ROLE OF UTERINE ARTERY DOPPLER IN EARLIER PREDICTION OF RESOLUTION IN POST MOLAR PREGNANCY SURVEILLANCE

DISSERTATION SUBMITTED FOR

M.S (BRANCH – II)

OBSTETRICS & GYNAECOLOGY

APRIL 2017

MADURAI MEDICAL COLLEGE, MADURAI

THE TAMILNADU Dr.M.G.R.MEDICAL UNIVERSITY

CHENNAI

CERTIFICATE

This is to certify that the dissertation entitled "**ROLE OF UTERINE ARTERY DOPPLER IN EARLIER PREDICTION OF RESOLUTION IN POST MOLAR PREGNANCY SURVEILLANCE"** is bonafide record work done by **Dr.NIVEDHITHA.S** under my supervision and guidance in the department of Obstetrics and Gynaecology, Madurai Medical College, during the academic year 2014-2017, submitted to The Tamilnadu Dr. M.G.R Medical University,by Dr.Nivedhitha.S in partial fulfillment for the award of the degree of M.S.(Obstetrics & Gynaecology) branch II.

Prof.Dr.M.VAIRAMUTHU RAJU, M.D.
Dean,
Government Rajaji Hospital,
Madurai Medical College,
Madurai.

Prof.Dr.C.SHANTHI,M.D.,DGO,FICOG.,
Professor & Head of the department,
Department of Obstetrics&Gynaecology,
Government Rajaji Hospital,
Madurai medical college,
Madurai.

DECLARATION

I **Dr. NIVEDHITHA.S** solemnly declare that the dissertation titled "**ROLE OF UTERINE ARTERY DOPPLER IN EARLIER PREDICTION OF RESOLUTION IN POST MOLAR PREGNANCY SURVEILLANCE"** has been prepared by me at The Department of obstetrics and gynaecology, Government Rajai Hospital, Madurai medical college, Madurai, under the guidance of **Prof. Dr. JOTHI SUNDARAM, M.D.,DGO**., Professor of obstetrics and gynaecology. I also declare that this bonafide work has not been submitted to any university for the award of any degree or diploma.

This is submitted to The Tamilnadu Dr, M.G.R Medical University, and Chennai in partial fulfillment of the regulations for the award of the degree of M.S., Branch II (Obstetrics & Gynaecology) examination to be held on April 2017.

Place : Madurai **Dr. NIVEDHITHA.S**

Date :

ACKNOWLEDGEMENT

I am extremely thankful to **Prof. Dr.M.VAIRAMUTHU RAJU, M.D.,** Dean, Madurai medical college, Madurai for his permission to carry out this study.

I am extremely thankful to **Prof. Dr.C.SHANTHI,M.D.,DGO.,FICOG.,** Head of the Department of Obstetrics & Gynaecology, Madurai Medical College, Madurai, for her expert guidance and support for the completion of the study.

I am immensely thankful to my guide **Prof. Dr.JOTHI SUNDARAM,M.D.,DGO.,** for her immense help and guidance in completion of the study.

I am sincerely thankful to **Prof. Dr.K.S.CHITRA,M.D.,DGO.,DNB OG., Prof.Dr.N.SUMATHI,MD,DGO., Prof.Dr.N.K.MAHALAKSHMI,MD,DGO., Prof.Dr.M.GAYATHRI,M.D OG.,** for their support, valuable advice and guidance in the analysis and successful completion of the study.

I thank all the assistant professors of the department of obstetrics and gynaecology for their guidance and kind help. I thank my beloved Husband and my parents for their continuous support from the very beginning of the study till the completion of the work.

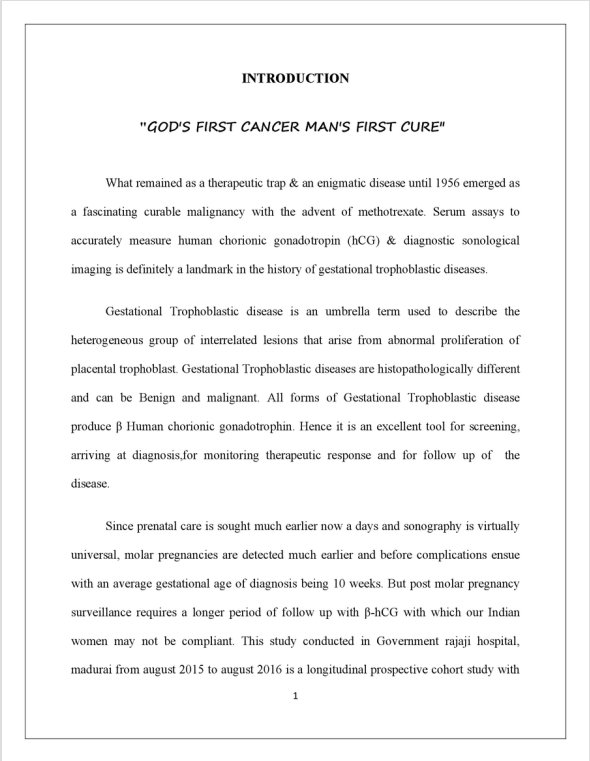
I acknowledge with thanks the cooperation of the patients without whom this study would not have been possible.

Digital Receipt

This receipt acknowledges that Turnitin received your paper. Below you will find the receipt information regarding your submission.

The first page of your submissions is displayed below.

Submission author:	221416101 Ms Og NIVEDHITHA.S
Assignment title:	2015-2015 plagiarism
Submission title:	Role of uterine artery doppler in ea..
File name:	6_final_image_removed.docx
File size:	392.11K
Page count:	86
Word count:	9,699
Character count:	54,501
Submission date:	23-Sep-2016 09:35PM
Submission ID:	707928103



INTRODUCTION

"GOD'S FIRST CANCER MAN'S FIRST CURE"

What remained as a therapeutic trap & an enigmatic disease until 1956 emerged as a fascinating curable malignancy with the advent of methotrexate. Serum assays to accurately measure human chorionic gonadotropin (hCG) & diagnostic sonological imaging is definitely a landmark in the history of gestational trophoblastic diseases.

Gestational Trophoblastic disease is an umbrella term used to describe the heterogeneous group of interrelated lesions that arise from abnormal proliferation of placental trophoblast. Gestational Trophoblastic diseases are histopathologically different and can be Benign and malignant. All forms of Gestational Trophoblastic disease produce β Human chorionic gonadotrophin. Hence it is an excellent tool for screening, arriving at diagnosis,for monitoring therapeutic response and for follow up of the disease.

Since prenatal care is sought much earlier now a days and sonography is virtually universal, molar pregnancies are detected much earlier and before complications ensue with an average gestational age of diagnosis being 10 weeks. But post molar pregnancy surveillance requires a longer period of follow up with β-hCG with which our Indian women may not be compliant. This study conducted in Government rajaji hospital, madurai from august 2015 to august 2016 is a longitudinal prospective cohort study with

1

CONTENTS

INTRODUCTION

"GOD'S FIRST CANCER MAN'S FIRST CURE"

What remained as a therapeutic trap & an enigmatic disease until 1956 emerged as a fascinating curable malignancy with the advent of methotrexate. Serum assays to accurately measure human chorionic gonadotropin (hCG) & diagnostic sonological imaging is definitely a landmark in the history of gestational trophoblastic diseases.

Gestational Trophoblastic disease is an umbrella term used to describe the heterogeneous group of interrelated lesions that arise from abnormal proliferation of placental trophoblast. Gestational Trophoblastic diseases are histopathologically different and can be Benign and malignant. All forms of Gestational Trophoblastic disease produce β Human chorionic gonadotrophin. Hence it is an excellent tool for screening, arriving at diagnosis, for monitoring therapeutic response and for follow up of the disease.

Since prenatal care is sought much earlier now a days and sonography is virtually universal, molar pregnancies are detected much earlier and before complications ensue with an average gestational age of diagnosis being 10 weeks. But post molar pregnancy surveillance requires a longer period of follow up with β-hCG with which our Indian women may not be compliant. This study conducted in Government rajaji hospital, Madurai from august 2015 to august 2016 is a longitudinal prospective cohort study with its aim to prove that uterine artery Doppler

changes can predict resolution or persistence of the disease much earlier when compared with serial β-hCG follow up, so that uterine artery Doppler monitoring can be an equivalent or a better alternative for β-hCG in predicting the course of the disease well ahead.

AIM OF THE STUDY

Our aim of the study is to evaluate the role of uterine artery Doppler in earlier prediction of resolution in post molar pregnancy surveillance compared to serial β-hCG follow up.

HYDATIDIFORM MOLE

DEFINITION:

In Latin the word **"hydatid"** means **"drop of water"** and the word **"mole"** means **"spot".**

Pathologically, *Hydatidiform moles are* nothing but placentas with abnormally developed chorionic villi with varying amount of proliferative trophoblast with an enlarged, edematous and vesicular appearance.

Trophoblast is comprised of

- Cytotrophoblast – have an increased mitotic index and do not produce any hormone.
- Syncytiotrophoblast- shows decreased mitotic index, produces beta-human chorionic gonadotrophin (β--hCG) and constitutes the chorionic villi.
- Intermediate trophoblast- marker of endometrial implantation and invasion.

Varying amount of proliferation of each kind of trophoblast constitutes the spectrum of gestational trophoblastic diseases.

WHO Classification[3]

<u>Premalignant Diseases</u>

- Complete Hydatidiform Mole (CM)
- Partial Hydatidiform Mole (PM)

Malignant Diseases (Gestational Trophoblastic Neoplasia)

- **Nonmetastatic**
    1. Invasive Mole
    2. Placental site trophoblastic tumor (PSTT)
- **Metastatic**
    1. Gestational Choriocarcinoma

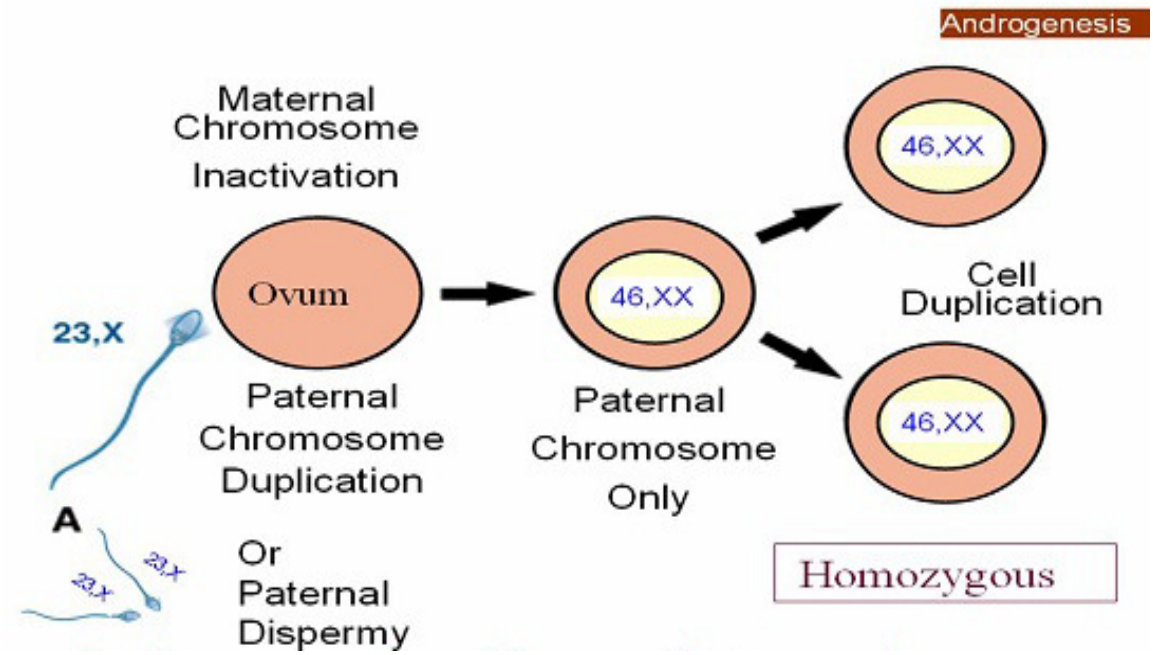
EPIDEMIOLOGY[1]

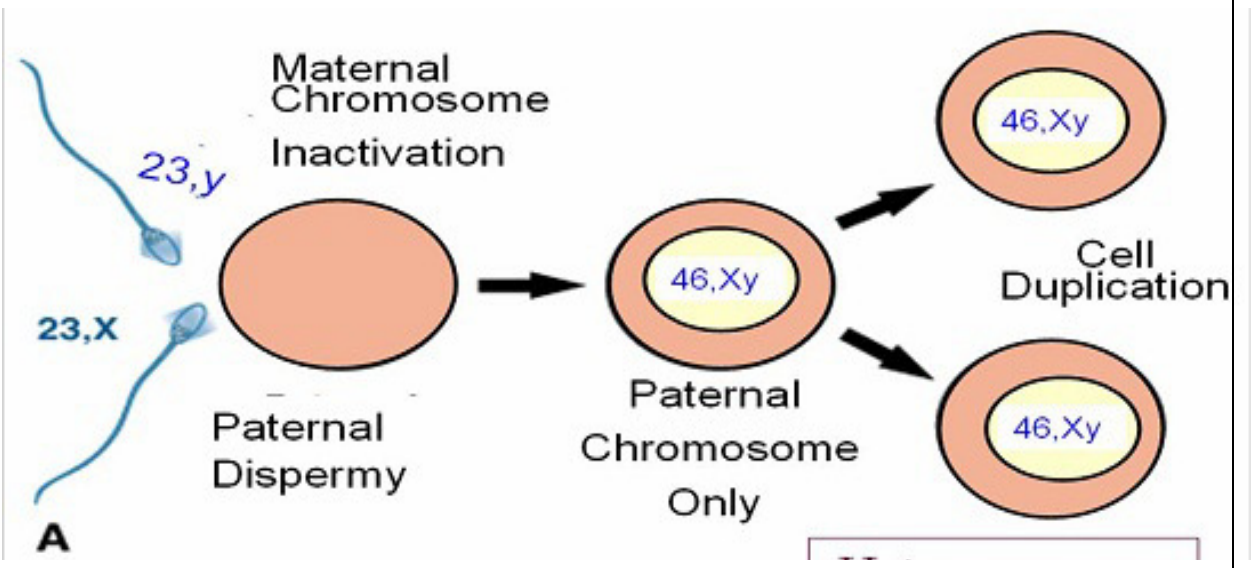
- Gestational trophoblastic diseases are common **in oriental countries-** Philippines, China, Indonesia, Japan, India, Central and Latin America and Africa.
- **India- 1 in 400 pregnancies**
- Calculated Incidence of **complete mole- 1 in 1945** pregnancies **partial mole- 1 in 695** pregnancies
- Age –Complete moles are most common at the extremes of reproductive age groups.
- The incidence of complete mole rises from 1: 1000 to 1:76; 1:6.5 in subsequent pregnancies.

PATHOPHYSIOLOGY:

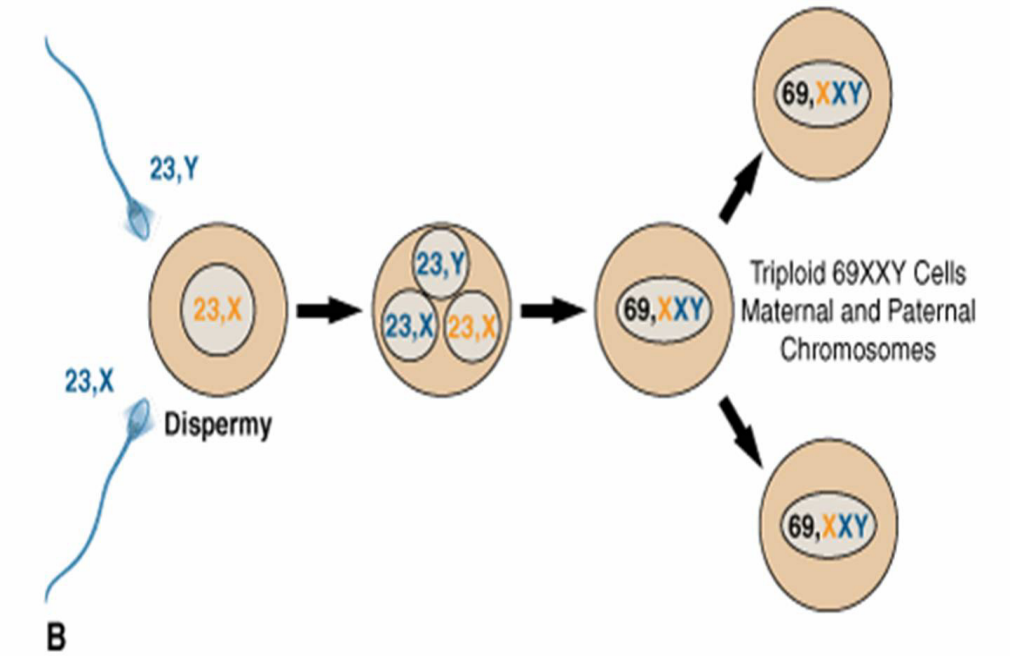
- Molar pregnancy arises due to aberrant fertilization process.
- Complete mole is androgenetic with a diploid karyotype.

Abnormal genetic event in complete mole





Abnormal genetic event in partial mole

- 

- The abnormal genetic event: Single haploid sperm (23X) and a chromosomally empty ovum undergo fertilization followed by duplication of chromosomes and zygote formation.
- There is no maternal contribution-DIANDRIC DIPLOIDY (46 XX).
- Occasionally two different sperms may fertilize an empty ovum- DIANDRIC DISPERMY (46XX, 46XY).
- Partial moles are usually triploid, formed when two paternal haploid chromosomes fertilize a maternal haploid-DISPERMIC FERTILIZATION or when a maternal haploid is fertilized by an unreduced diploid sperm-DIANDRIC TRIPLOIDY
- Fetal parts and placenta are seen in partial moles.
- Complete moles have more tendency of persistence and malignant transformation than partial moles.

GENETICS:

- *P57 cycline* dependent kinase inhibitor is paternally imprinted gene which is maternally expressed.
- ***P57 kip2*** **immunostaining is** negative in complete mole in contrast to Partial mole, Hydropic abortions & normal placenta.
- Abnormal Methylation.
- In cases of Familial recurrent molar pregnancy; Defective locus at **19q 13.4** at single gene NALP7, it is member of CATERPILLAR family involved in inflammation & Apoptosis in genetic Complete mole.

- Three other genes **H19, P57, IGF-2.**
- Chorio CA-specific genes deletion **7p12-q11.2;** Amplification of **7q21-q31** region; loss of **8p12-p21.**
- HTERT—human telomerase reverse transcriptase expression in uterine contents of cases of complete mole is suggested as a marker for persistent disease and malignant transformation.

CLINICAL PICTURE[1]:

Conventionally complete mole was diagnosed with the following features,

- Abnormal Bleeding per vaginum-commonest presentation,
- Hyperemesis (10%),
- Early onset gestational hypertension (5%,),
- Anemia,
- Uterine size large for date (25%),
- Hyperthyroidism (10%),
- Pulmonary trophoblostic emboli,
- Prominent theca lutin cyst.

Partial mole presented with less severe symptoms more often diagnosed as missed abortion or incomplete miscarriage.

But nowadays, since prenatal care is sought much earlier and sonography is virtually universal, the clinical presentations have changed remarkably with earlier reduction and before complication ensue. The mean of diagnosis is at around ten weeks.

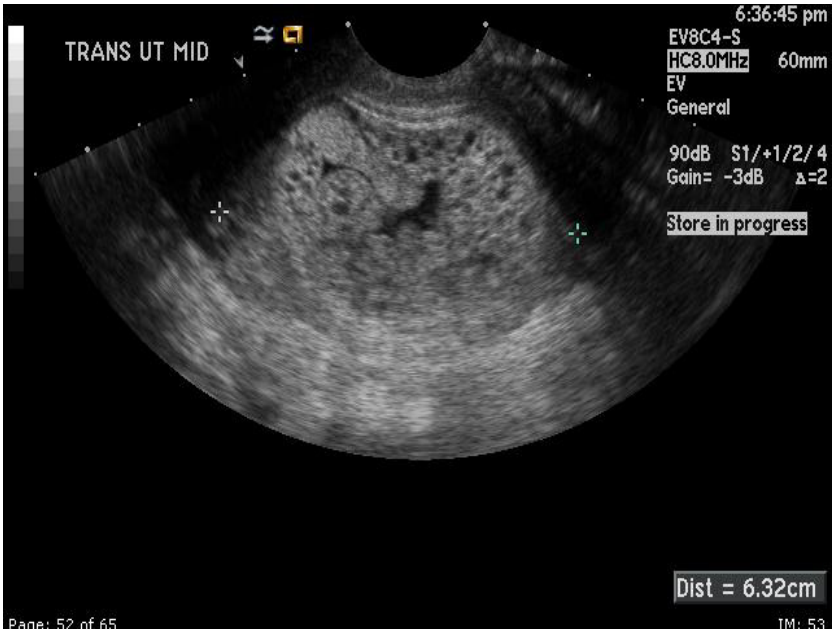
SONOGRAPHY:

Sonagraphic imaging remains the mainstay of diagnosing gestational trophoblastic disease. The accuracy of pre evacuation diagnosis of molar pregnancy increases with increasing gestational age.

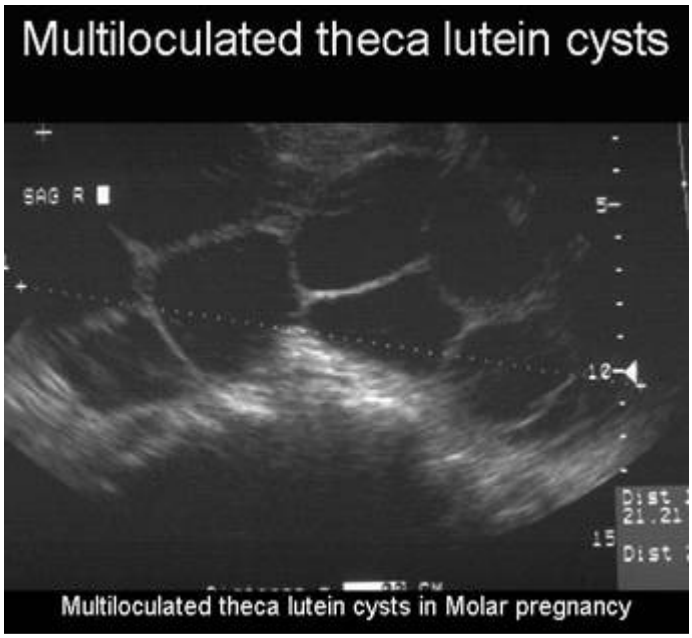
Complete Hydatidiform Mole[10]

- UTERINE SIGNS
  i) Uterine enlargement-60%,
  ii) Echogenic mass in endometrial cavity,
  iii) Multiple discrete anechoiec cystic areas with heterogeneous echogenicity in the centre - **SNOW STORM APPEARANCE-** seen in <2/3^{rds} of cases, less common in first trimester
- OVARIAN SIGNS:
  i) Enlarged ovaries,
  ii) Theca lutein cyst- due to hyper stimulation from raised circulating hcg levels.
  iii) Theca lutein cysts are often bilateral and multiloculated, do resolve with treatment, very rarely may present with hemorrhage or rupture.

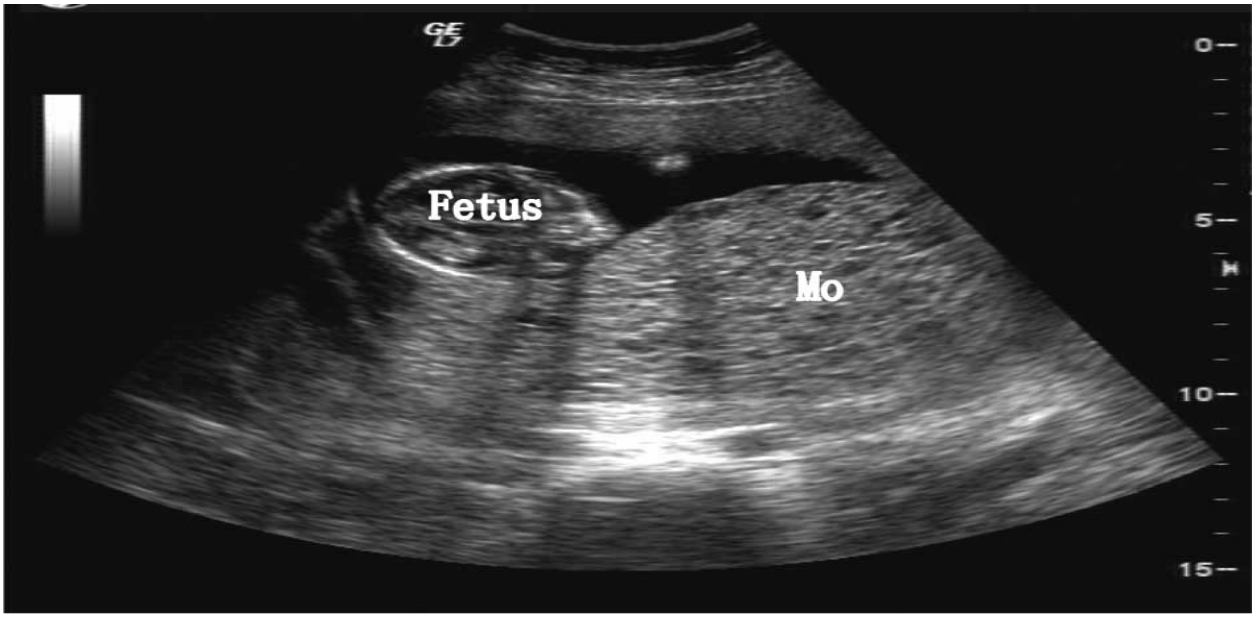
SNOW STORM APPERANCE of the Complete Mole



Theca lutein cyst



Sonographic appearance of Partial mole



Partial Hydatidiform Mole

- Partial hydatidiform mole is sonographycally seen as cystic spaces in the placenta and the gestational sac has transverse to antero-posterior diameter of more than 1.5.
- Fetus may still be viable but with unusual growth restriction or developmental abnormalities.
- ß-hCG in women with complete Hydatidiform mole, the total hCG values exceed 1 lakh IU/L. But in partial molar pregnancy hcg levels are within wide range associated with normal pregnancy.

Role of Doppler:

- Uterine artery Doppler study in early trimester of a normal pregnancy shows increased resistance with low diastolic waveforms except for the implantation site.
- With increasing gestational age, there is a gradual fall in resistance indices due to physiological trophoblastic arterial invasion.
- But In molar pregnancy, uterine artery Doppler studies show reduced resistance indices with high velocity Doppler waveforms, due to much higher degree of arterial invasion by abnormally proliferating trophoblastic tissues.
- Myometrial Invasion is seen as chaotic mass with loss of vascular delineation due to arterio venous shunts and neovascularization.
- High resistance index after evacuation indicates completeness of evacuation.
- Low resistance index is an adverse prognostic indicator.

MANAGEMENT OF GESTATIONAL TROPHOBLASTIC DISEASE

Preoperative work up

- Complete blood count,
- Platelets,
- Clotting time ,
- Liver function tests
- BUN,
- Serum creatinine
- Serum electrolytes
- Thyroid Profile
- Chest X ray
- B-hCG
- Ultrasound with Doppler

Termination

- Regardless of uterine size **suction evacuation** is the management.
- Medical evacuation of CHM should be avoided due to the risk of embolisation.
- Pre operative cervical dilatation with osmotic agents like **laminaria tent.**
- **Prostaglandins and oxytocin induction is not recommended** due to the risk of bleeding and trophoblastic embolisation.

- Cervix should be mechanically dilated to allow the insertion of 10-14 mm suction cannula.
- IV oxytocin should be started after dilatation of the cervix at the initiation of suctioning and continued postoperatively to reduce the likelihood of hemorrhage.
- Some degree of trophoblastic deportation into the pelvic venous system takes place during molar evacuation.
- With the large mole –the volume of the tumor may be significant, to produce respiratory distress /pulmonary edema.
- Respiratory distress is treated with the assisted ventilation and monitoring is required.
- Because of deportation trophoblast will thrive within lung parenchyma to cause persistent disease and even overt malignancy.
- Re evacuation of retained molar tissues should never be done.
- Anti D is mandatory if the mother is Rh negative.
- Histo pathological examination of the products evacuated should be routinely done.
- A check ultrasound with uterine artery resistance index is done at 48 hours post evacuation along with B -hCG.

High Risk For Developing Post molar tumor

- hCG Levels > 100,000 mIU/L
- Uterine Enlargement > 16 weeks
- Theca leutin cyst of more than 6 cm in size

Post suction evacuation follow up:

- ß-hcg within 48 hours after evacuation.
- Once weekly until two normal values.
- Once in a month after normal level obtained for six months
- The protocol for follow up is individualised for each patient based on the type of Gestational Trophoblastic Disease.
- Patients are followed up in GTD clinic once pathologist confirmed diagnosis.

i. Partial mole: followed up until β-hCG becomes negative

ii. Complete mole: Until 6 months after normal values are obtained

iii. Vesicular mole with multiple pregnancy: monthly follow up for 12 months

In this study the patients were followed up with serial β -hCG at 48 hours, 2^{nd} ,4^{th},8^{th} week post evacuation, since the average time for normalization of β- hCG post evacuation is around 8- 9 weeks.

If no pathology report is available, then assume as complete mole and follow up 6 months after normalisation. During each follow up, thorough gynaecological examination and contraception advice given as,

- Should NOT conceive until follow up is complete.
- Use Barrier method until hCG becomes normal
- Use of combined oral contraceptive pill after normalisation of β- hCG.
- IUCD are contraindicated due to increased tendency of uterine perforation.

CLINICAL FEATURES OF GESTATIONAL TROPHOBLASTIC NEOPLASIA[1]

Invasive Mole:

- Clinical diagnosis by plateau or rising titers of β-hCG in the weeks after molar evacuation & USG.
- Persistent bleeding p/v
- Lower abdominal pain due to invasion in myometrium, vulva, vagina or intra abdominal metastasis.
- It may spread to adjacent pelvic structures, bladder and rectum causing hematuria, and bleeding per rectum.
- Pulmonary metastasis.

Placental Site Trophoblastic Tumor (PSTT):

- Rare slow growing tumor,
- Mainly from intermediate trophoblast,
- Menstrual irregularities & lower abdominal pain, galactorrhea due to hyperprolactinemia increased h PL
- Little or no h CG is produced (Free B hCG fragment)
- Rarely presents as nephrotic syndrome, hematuria or DIC
- Spread is late, local Infiltration & metastasis is through lymphatic channels.

Choriocarcinoma:

- Occurs following any form of pregnancy, **mainly after complete mole.**
- Clinical features of bleeding p/v, lower abdominal pain, or in 1/3 of cases no pelvic symptoms but symptoms of distant metastasis to lungs, brain, liver, skin, cauda equina & the heart may present.
- Highly malignant, appears as soft purple largely hemorrhagic mass.
- Microscopic: implanting blastocyst with central cores of mononuclear cytotrophoblast surrounded by rim of multinucleated syncytiotrophoblast & distinct absence of chorionic villi with extensive areas of necrosis & hemorrhage &frequent evidence of tumor in the sinuses.

- The hypervascularity & absence of connective tissue support are the reason for its highly malignant behavior.

NON GYNAECOLOGICAL PRESENTATIONS OF GESTATIONAL TROPHOBLASTIC NEOPLASIA[1]:

Central Nervous System

- Sudden collapse or loss of consciousness due to intracranial hemorrhage,
- Epilepsy/visual field defects,

Cardio Vascular System

- Acute embolic complication,
- Pulmonary hypertension,
- Very rarely intracavitory tumor of left atrium presenting similar to left Atrial myxoma.

Respiratory System

- Respiratory failure,
- Intrathoracic hemorrhage.

Gastro Intestinal System

- Massive hemoperitonium,
- GI bleed secondary to esophageal, gastric and small bowel metastasis.

Genitourinary System

- Hematuria
- Oliguria

- Abdominal pain
- Retroperitonal hemorrhage

INVESTIGATIONS:

- Quantitative beta hCG
- X Ray Chest
- Pelvic Doppler USG
- Abdominal Doppler USG to rule out liver & renal metastasis
- CT chest , abdomen
- MRI brain
- Beta hCG in cerebrospinal fluid
- PET
- Genetic studies

FIGO REQUIREMENT FOR MAKING DIAGNOSIS OF GTN

1. Four values or more of plateau hCG over at least 3 weeks: days 1, 7, 14 and 21.
2. A rise of hCG of 10% or greater for 3 values or more over at least 2 weeks: days 1, 7, and 14.
3. Histological diagnosis of choriocarcinoma.
4. Persistence of hCG beyond 6 months after mole evacuation.

ANATOMIC FIGO STAGING SYSTEM FOR GTN (2000)[1]

Stage	*Criteria*
I.	*Disease confined to the uterus*
II.	*Disease outside of uterus but is limited to the genital structures*
III.	*Disease extends to the lungs with or without known genital tract involvement*
IV.	*All other metastatic sites*

Table 1 Modified prognostic WHO scoring system as adapted by FIGO

Scores	0	1	2	4
Age	<40	>40	–	–
Antecedent pregnancy	Mole	Abortion	Term	–
Interval from pregnancy	<4 months	4-6 months	7-12 months	>12 months
Pretreatment serum HCG (IU/L)	<103	103-104	104-105	>105
Largest tumor size including uterus	<3 cm	3-4 cm	5 cm or more	–
Site of metastasis	Lung	Spleen, kidney	GI system	Liver, brain
Number of metastasis	–	1-4	5-8	>8
Previously failed chemotherapy	–	–	Single drug	2 or more drugs

LOW RISK GTN:

- FIGO score 6 or less.
- Drugs schedules: single agent chemotherapy

Most commonly used regimen:-

Methotrexate: 1 mg/kg 1M on days 1, 3, 5, 7

Folinic acid 0.1 mg/kg 1M on days, 2, 4, 6 and 8.

Side Effects: Stomatitis, conjunctivitis, abdominal and chest pain.

Actinomycin- D: (primary therapy in case of abnormal liver function)

After the first treatment

- Further chemotherapy is withheld as long as the HCG level is falling progressively
- Additional single agent chemotherapy is not administered at any predetermined or fixed interval

II course of Chemotherapy if:

- If HCG level plateaus for more than 3 consecutive weeks or begins to rise again.
- If HCG level does not decline by 1 log within 18 days of completion of first treatment,

- If response to first treatment was inadequate, dose of MTX is increased from 1mg/kg/day to 1.5 mg/kg/day for each of the 4 treatment days.

HIGH RISK GTN:

- Stage I, II, III With FIGO score 7 or greater or Stage IV
- Treated with primary intensive combination chemotherapy
- Regimes given are :
  - MAC.
  - Modified Bagshawe (CHAMOCA)
  - EMA-CO
  - EMA-EP.

MAC III REGIMEN

Methotrexate 1 mg/kg IM/1V		Days 1, 3, 5, 7
Folinic acid	0.1 mg/kg IM	Days 2, 4, 6, 8
Actinomycin-D 12 μg/kg IV		Days 1-5
Cyclophosphamide	3 mg/kg IV	Days 1-5

To be repeated every 15 days if no signs of toxicity.

EMA CO REGIMEN

Etoposide, methotrexate, actinomycin D, alternating weekly with cyclophosphamide and oncovin.

Day 1

Actinomycin D 500 micrograms IV push,

Etoposide IV 100 mg/m^2 over 30-50 min.

Methotrexate 100 mg/m^2 IV infusion over 1 hr and

Methotrexate 200 mg/m^2 IV infusion over 12 hrs

Day 2

Actinomycin D 500 micrograms IV push

Etoposide 100 mg/m^2 IV over 30-50 min.

Folinic acid 15 mg IV push for every 6 hours for 8 doses beginning 24 hours after methotrexate bolus.

Day 8

Vincristine (Oncovin) 1 mg/m^2 IV

Cyclophosphamide 600 mg/m^2 IV

SIDE EFFECT:- Myelosuppresion ,Mucositis , Neuropathy ,Reversible alopecia

EMA-EP REGIMEN

- In patient resistant to EMA-CO

  On day 8

- Etoposide- 10 mg/m2 iv.
- Cisplatin- 80 mg/m2 iv
- treatment – until 3 consecutive weekly titers normal.
- 2-4 cycles given further after initial normal β -hCG.

Management of sites of metastasis

VAGINAL &PELVIS (30%)-

- Single agent chemotherapy –for Low risk GTN
- Combination chemotherapy –for High risk GTN
- If bleeding occurs-
    - Vaginal packing
    - Wide local excision
    - Arteriographic embolisation of hypogastric arteries.

PULMONARY(80%):

- Present as – Chest pain, cough, hemoptysis dyspnoea.
- X-ray features- Snowstorm
- Discrete round densities.
- Pleural effusion
- Embolic pattern

Treatment:

- Single agent chemotherapy-for low risk GTN.
- Combination –for high risk GTN.
- Thoracotomy- if pulmonary parenchyma is viable.

HEPATIC (10%):

- Worse prognosis.
- Usually associated with widespread metastasis Intraperitoneal bleeding may occur.

Treatment:

- Chemo & concurrent radiation (2000-3000 cGy).
- Hepatic resection to excise resistant foci.

CEREBRAL-10%

- Acute focal neurological deficits.
- Combination chemo + WBRT (2000-3000).
- Patients with metastasis on initial evaluation respond better than who develop Lesion during therapy.
- During period of WBRT- Methotrexate in EMA-CO be increased to 1 g/m^2 with Folinic acid rescue.

For subsequent pregnancy.

- Ist trimester TVS to confirm normal pregnancy.
- β-hCG 6 wks after termination of pregnancy .

- After effective treatment for non-malignant GTN molar pregnancy occur in 2-10% subsequent pregnancies.

HUMAN CHORIONIC GONADOTROPIN

Human chorionic gonadotropin (hCG) is a heterodimeric glycoprotein composed of 237 amino acids with a molecular weight of 25.7 kDa, produced by human placental syncytiotrophoblast. It has an α (alpha) subunit and β (beta) subunit. The α (alpha) subunit is similar to luteinizing hormone, follicle-stimulating hormone, and thyroid-stimulating hormone. The β (beta) subunit is unique to hCG. Other forms of human chorionic gonadotropin may be present in serum such as nicked hCG, Free β subunit, Nicked free β subunit, β subunit without C terminal peptide and β core fragment.

The hormone Human chorionic gonadotropin promotes and maintains the corpus luteum during early pregnancy by interacting with the **luteinizing hormone/choriogonadotropin receptor** (**LHCGR**) of the ovary, so that the corpus luteum secretes progesterone during the first trimester. Progesterone inturn enriches the uterus with a thick lining of blood vessels and capillaries to sustain the growing fetus.

Being secreted by placental syncytiotrophoblast, the β human chorionic gonadotropin hormone is commonly called as "The pregnancy hormone". Though the presence of β-hCG in urine or serum almost always indicates pregnancy, it can be produced in the absence of an embryo.

β human chorionic gonadotropin can be detected in maternal urine and plasma as early as 6 to 9 days after ovulation. There is an exponential increase in hCG level

with a doubling time of 1.5 days in first 6 weeks, peaks around 1 lakh IU/L at 8 to 10 weeks, starts decreasing from 12^{th} week and plateaus at approximately 30000 IU/L from 20^{th} week until term. In the postpartum period β hCG shows a slower decline than intact hCG. All forms of gestational trophoblastic disease produce high levels of hCG except for placental site trophoblastic tumor. Hence serial hCG measurement is a well known indicator and predictor of the course of the disease, reassuring sustained remission, recognizing relapse, and malignant transformation.

Hyperglycosylated hCG, produced by cytotrophoblast is found in

- Normal pregnancy
- Invasive mole

Elliott et al has proved that four O linked oligosaccharides are the main difference between hCG produced by malignancy and normal pregnancy. Lower proportion of hyperglycosylated hCG is associated with early pregnancy loss.

MEASUREMENT OF hCG

The conventionally used radioimmuno assays based on serum antibodies against intact hCG has low specificity due to high cross reactivity with leutinizing hormone, following which radioimmuno assays using polyclonal antibodies, specifically against β-hCG came into use. Sandwich type assays detect intact hCG only and hence they are highly specific.

False positive hCG suspected if

- hCG level plateau at low concentration
- failure to respond to chemotherapy

Unnecessary treatment of presumed persistent trophoblastic disease can be avoided by urinary hCG measurement as these heterophilic antibodies are not excreted in urine.

Persistent low elevation of β hCG without clinical evidence of active gestational trophoblastic disease is seen in

- Quiescent gestational trophoblastic neoplasia
- Pituitary derived hCG
- Nongestational neoplasia
- Physiological elevation

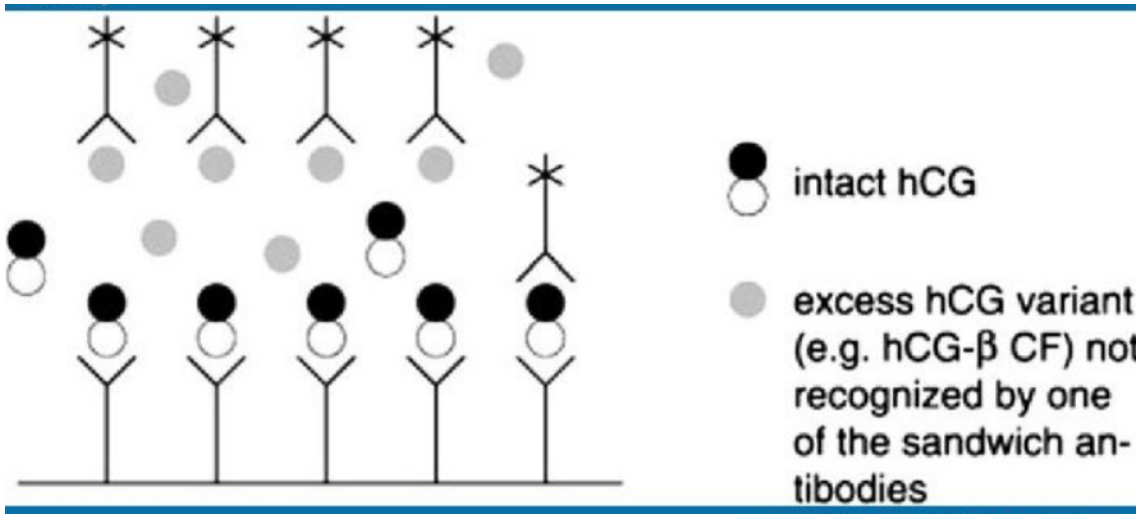
OTHER BIOCHEMICAL PREDICTORS OF PERSISTANT TROPHOBLASTIC DISEASE

Biomarkers like progesterone, inhibin A, Activin A, Human placental lactogen, CA 125, Carcinoembryonic antigen, CA 15-3, CA 19-9, Leptin, 17- β estradiol are under study as predictors of persistent trophoblastic disease.

HOOK EFFECT

- Hook effect first was described by Miles et al in 1976. Very high values can lead to erroneous false negative UPT because of oversaturation of the test assay by excessive β-hCG hormone—known as hook effect.

- False negative qualitative βhCG assay in the above scenario was caused by the high dose hook effect.
- hCG level in the order of 1×10^9 IU/ml is necessary for high dose hook effect to occur.
- High dose hook effect occurs whenever there is a inordinate amount of a substance being measured by an immune assay causing incomplete antigen and antibody complexes to form.
- Below a certain threshold concentration the assay will reflect accurately the raising concentration of the substance.
- Past the threshold concentration when incomplete complexes begin to form the assay will form falsely lower readings as the concentration rises higher and higher



DURATION OF FOLLOWUP

The duration of follow up should be dependent on type of GTD. This follow up plan can be followed in GTD clinic once pathologist confirmed diagnosis.

- Partial mole : stop as soon as β-hCG negative
- Complete mole: 6 months after normalisation
- Any mole with multiple pregnancy : monthly for 12 months,

If no pathology report is available, then assume as complete mole and follow up 6 months after normalisation.

THE ULTRASONOGRAM

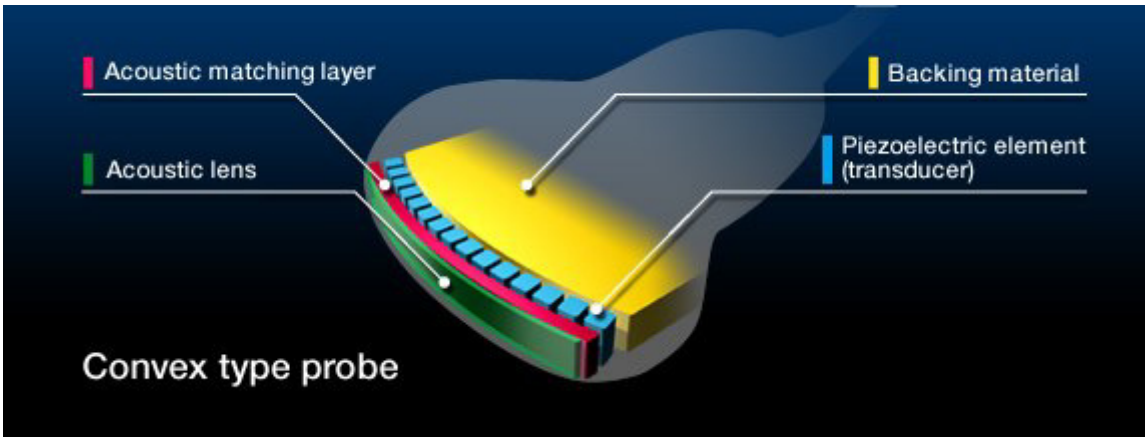
Over half a century ultrasound has been extensively used to image human body. It was first used as a medical diagnostic tool to image brain by an Austrian neurologist, Dr.Karl Theodore Dussik in 1942. Later the practical technology and its application have been developed by Prof Ian Donald from Scotland. Now a days ultrasound became one of the most extensively used imaging technologies since it is portable, free from radiation risk, and inexpensive. Ultrasound images are tomographic and can be real time.

PRINCIPLES

The working principle of ultrasonogram is based on piezoelectric effect, which was discovered by the Curie brothers in 1880 when they subjected quartz to mechanical stress generating an electrical charge on the surface. They also discovered reverse piezoelectric effect by electrical application produces vibration on quartz.

Pulse – Echo approach is the working principle in modern medical ultrasonogram. The piezo electric crystals in ultrasound transducer are capable of producing small ultrasound pulses on electrical stimuli. These pulse waves penetrate body tissues of different acoustic impedance. Some waves are reflected back to transducer, some penetrates deeper, and some waves are scattered. The returned echo signals are combined and processed to produce an image. Hence the ultrasound transducer works as both pulse generator and microphone.

Parts of ultrasound transducer



Curved array transducer

Linear array transducer

Phased array Transducer

Transvaginal transducer

The frequencies of ultrasound waves are beyond upper limit of audible human hearing i.e. more than 20 kHz. Audible human hearing ranges between 20 – 20000Hz. The frequency of ultrasound waves used in most medical devices ranges between 1 - 20 MHz.

MACHINE COMPONENTS

1. THE TRANSDUCER

The ultrasound transducer consists of backing material, piezoelectric elements, Electrodes and Acoustic lens.

The transducer converts

- Electricity--Piezoelectric element oscillation—ultrasonic waves
- Ultrasonic waves --Piezoelectric element –electricity

➢ **Types**

- Curved array

A curvilinear probe uses low frequency ultrasound waves to produce less resolution images than linear probe.

- Linear array

A linear probe uses high frequency ultrasound to produce high resolution images of superficial structures.

- Phased array

It gives more depth to allow deep structures through small acoustic window.

2. **CPU**
3. **CONTROL PANEL**
4. **MONITOR**

DISPLAY MODES

- B mode – gives two dimensional images
- M mode – gives two dimensional image and allows motion recording
- Doppler – measures frequency shift in echo
- Colour Doppler – colours are used corresponding to frequency shift.

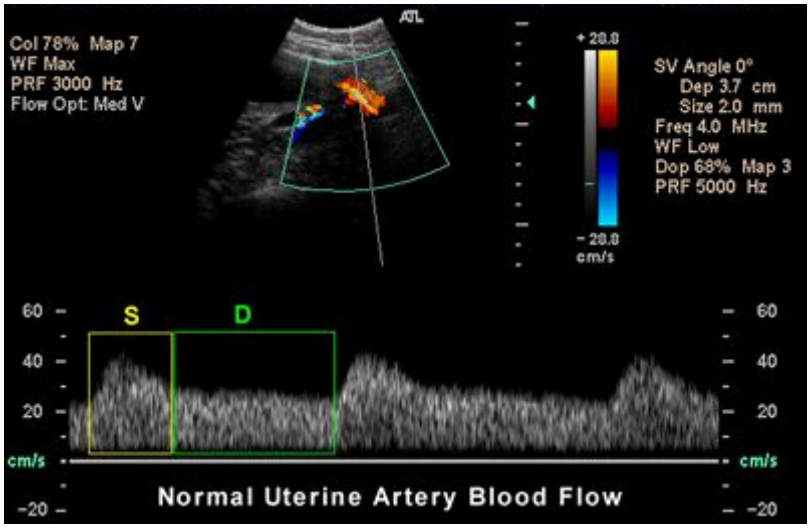
  Red –blood flow toward the probe

  Blue –blood flow away from the probe.

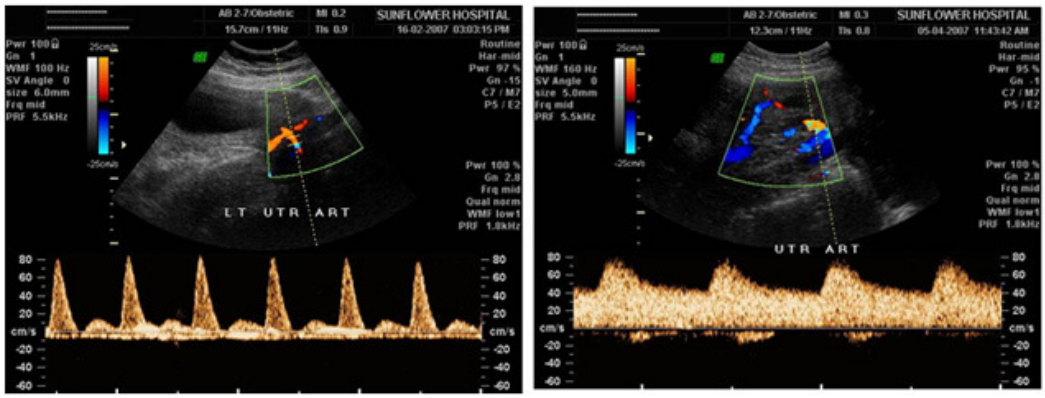
DOPPLER ULTRASONOGRAM

Ultrasound Doppler images, whether color Doppler or spectral Doppler, are essentially obtained from measurements of movement. From ultrasound transducers, a series of pulses is transmitted to detect movement of blood. Echoes from stationary tissue are the same from pulse to pulse. But echoes from moving objects exhibit slight differences in the time for the signal to be returned to the receiver. These differences are measured as the 'Doppler frequency' and are processed to produce either a color flow display or a Doppler sonogram.

Uterine artery Doppler shows normal blood flow



Uterine artery Doppler showing high resistance flow and low resistance flow respectively



UTERINE ARTERY RESISTANCE INDEX

The Doppler ultrasound is used to evaluate uterine artery by quantifying the waveform by measuring the blood flow velocity at peak systole (maximal contraction of the heart) and peak diastole (maximal relaxation of the heart). These values are then computed to derive a ratio called **Uterine Artery** Resistance **Index (UARI)** in which the peak of systole is divided by the sum of systole and diastole.

UARI= peak systole / (peak systole + peak diastole)

Uterine artery resistance index has been studied extensively in

- Prediction of development of gestational trophoblastic neoplasia
- Diagnosis of gestational trophoblastic neoplasia, low uterine artery Doppler indices seems to be correlated with invasive disease.
- Diagnosis of gestational trophoblastic neoplasia associated with methotrexate resistance.
- Detection of high risk pregnancies such as Preeclampsia.

In our study uterine artery resistance index has been tooled as a marker for earlier prediction of resolution in post molar pregnancy surveillance.

REVIEW OF LITERATURE

1. Neda Salih Amin et al [4], 2007

Neda Salih Amin et al conducted a longitudinal study in Al yarmouk teaching hospital from Jan 2006-07. About 25 cases of vesicular mole were assessed by measuring the serial β-hCG levels in the pre and post evacuation period and finding its relation with changes in the uterine artery blood flow using Doppler indices.

Out of these 25 cases, 22 patients had steady fall in serum β-hCG level and found to be normal at 6^{th} week of post evacuation and also showed a steady rise in the Doppler indices from the pre evacuation to 6^{th} week of post evacuation. 2 patients showed plateauing of all Doppler indices without any consistent decrease of β-hCG and were proved to be persistent gestational trophoblastic disease.

Neda salih Amin et al, concluded that there was a significant correlation between the serial β-hCG serum levels and uterine artery Doppler indices and suggested that Doppler indices may be used to predict and define the course of the disease.

2. Qi Zhou et al [5], 2004

Qi Zhou et al conducted a retrospective analytical study to evaluate the clinical utility of sonography with Doppler in the diagnosis and treatment of gestational trophoblastic diseases. Doppler examination of about 355 cases of molar pregnancy

diagnosed and treated at Xian Jiaotong University in china between 1991 and 2003 were analyzed in comparison with patients in normal early pregnancy.

Out of the 355 patients with gestational trophoblastic disease, 106 patients were diagnosed to have complete Hydatidiform mole, 33 patients were diagnosed to have partial Hydatidiform mole, 33 patients have choriocarcinoma, and 184 patients have invasive Hydatidiform mole.

Soft tissue invasion and cystic vascular spaces within the myometrium were the hallmark of invasive diseases. Complete mole had molar tissue confined to the endometrial cavity, while partial mole had thickened hydropic placenta along with the fetus.

In that study the uterine artery Doppler showed resistance indices for

- Complete Hydatidiform mole – 0.55 (SD 0.06)
- Partial Hydatidiform mole – 0.56 (SD 0.04)
- Invasive Hydatidiform mole – 0.28 (SD 0.06)
- Choriocarcinoma – 0.25 (SD 0.05)
- Normal pregnancy – 0.06 (SD 0.04)

With successful chemotherapy the sonographic and Doppler abnormalities of invasive disease resolved.

Qi Zhou et al concluded that the sonography and Doppler imaging are excellent tools for the diagnosis of disease, to detect invasion or recurrence and in following the effectiveness of chemotherapy.

3. Diaa Eldeen M Abd El Aal et al [8], 2003

Diaa Eldeen M Abd El Aal et al conducted a longitudinal study in Assiut university hospital to evaluate the correlation between Doppler blood flow and β-hCG to predict the course of the disease and follow up after hydatidiform mole evacuation.

15 cases of molar pregnancy were taken up for the study. B-hCG and uterine artery Doppler indices were studied the day before evacuation of uterus. Those cases were followed up every 2 weeks for first two months and every month for six months post evacuation.

Out of 15, twelve patients showed gradual decrease in β-hCG from 1192 $\pm$ 697 to 6 $\pm$ 11 IU/ml by the end of second month. The uterine artery resistance index increased from 0.55 $\pm$ 0.15 to 1.0 $\pm$ 0.26 and the pusatality index increased from 1.02 $\pm$ 0.47 to 6.12 $\pm$ 2.34.

Two patients showed a slower decrease in β hCG and one showed a fluctuating level of β hCG around the same level, while Doppler indices increased in post evacuation period for all 15 cases.

So the study concluded that Doppler ultrasonography can be used as an adjuvant tool in the follow up of hydatidiform mole and can predict the disease progression to invasive mole.

4. Lawrence H. Lin et al [6], 2015

Lawrence H. Lin et al published a review article on 2015 by reviewing studies evaluating the role of Doppler ultrasonography in the diagnosis, disease progression and follow up of patients with Gestational Trophoblastic Diseases.

28 studies conducted until 2014 were included for this review and concluded that Doppler ultrasonography findings were used as ancillary tools along with β hCG assessment in the diagnosis of gestational trophoblastic neoplasia. The uterine artery Doppler velocimetry used in the prediction of trophoblastic neoplasia and chemoresistance of trophoblastic neoplasia.

5. Flavia Tarabini Castellani Asmer et al [12], 2014

Flavia Tarabini Castellani Asmer et al, conducted a prospective cohort study at three trophoblastic centers in brazil between 2013 -2014,

- To Compare uterine artery velocimetry before and after complete hydatidiform mole evacuation between those women who develop post molar gestational trophoblastic neoplasia and those with spontaneous remission.
- To assess the usefulness of uterine artery Doppler indices as predictor of post molar gestational trophoblastic neoplasia.

246 patients with complete hydatidiform mole were included in the study. The pulsatality index (PI), resistive index (RI), and systolic/diastolic ratio (S/D) were measured pre evacuation of complete hydatidiform mole and 4 – 6 weeks post evacuation of complete hydatidiform mole along with serial β hCG.

The study results that, those patients who achieved spontaneous remission, the uterine artery Doppler indices were increased after evacuation. Those who developed post complete hydatidiform molar gestational trophoblastic neoplasia, the Doppler indices were decreased significantly.

Thus the study concluded that pre and post molar evacuation Doppler indices can be useful for predicting post molar gestational trophoblastic neoplasia.

6. Mahrooz malek et al [7],

Mahrooz malek et al, conducted a prospective study in 19 patients with gestational trophoblastic disease. Transvaginal ultrasound and Doppler findings were evaluated the day before evacuation and 1st week after evacuation, every 2 weeks for next two months and monthly for next 6 months. The study concluded that Doppler findings of molar pregnancy have capability to predict the disease progression.

7. Amit Kyal et al [13],

Amit Kyal et al conducted a prospective observational study in Kolkata medical college from 2011 to 2012 to correlate the uterine artery pulsatality index as a predictor for gestational trophoblastic neoplasia response to chemotherapy.

22 patients with gestational trophoblastic neoplasia were taken up for the study. All the cases were given inj.methotrxate 50mg im on 1,3,5,7 days with inj. folinic acid 15 mg im on 2,4,6,8 days. Chemotherapy was continued until β hCG becomes undetectable and further two more cycles were given.

B hCG concentration of these patients at the time of diagnosis ranged from 1400 – 210000 and Uterine Artery Pulsatality Index ranged from 0.47 – 2.1. The mean Uterine Artery Pulsatality Index before chemotherapy was 1.33 and at the end of 16 weeks was 1.952.

The study results that fall in β hCG is well correlated with rise in Uterine Artery Pulsatality Index. So concluded that Uterine Artery Pulsatality Index as an independent predictor for gestational trophoblastic neoplasia response to chemotherapy.

8. R Agarwal et al [9,]

R Agarwal et al conducted a prospective cohort study to evaluate Uterine Artery Pulsatality Index as a predictor of gestational trophoblastic neoplasia resistance to methotrexate. The study was conducted from 2008 to 2011 with 206 patients with gestational trophoblastic neoplasia. The mean Uterine Artery Pulsatality Index was lower in methotrexate resistance group compared to methotrexate response group.

The study concluded that Uterine Artery Pulsatality Index represents as an independent predictor of gestational trophoblastic neoplasia resistant to methotrexate.

MATERIALS AND METHODS

This study was conducted at Government Rajaji medical college and Hospital, Madurai. 40 patients with clinical & sonographic evidence of hydatidiform mole were included in the study after obtaining Ethics committee approval. Informed written consent was obtained from the patients who were included in the study.

STATEMENT:

To study the role of uterine artery Doppler in predicting the resolution of molar pregnancy earlier than serial β-hCG follow up

AIM OF THE STUDY:

- To study the changes in uterine artery doppler,before & after the evacuation of molar pregnancy along with serial β-hCG follow up
- To prove that Doppler can predict resolution 8 weeks before the disappearance of β-hCG, while persistence was indicated 1-3 weeks before the increase of β-hCG.

STUDY DESIGN:

Longitudinal prospective cohort study

PERIOD OF STUDY:

12 months

SAMPLE SIZE:

40 patients of molar pregnancy

PARTICIPANTS:

All cases of molar pregnancy recruited from outpatient clinic & hospital admissions.

INCLUSION CRITERIA:

1. Amenorrheic women presenting with clinical & sonographic evidence of hydatidiform mole,
2. Patients who have given informed consent to undergo the study,

EXCLUSION CRITERIA:

1. Not satisfying inclusion criteria
2. Lack of written informed consent
3. Chronic hypertension
4. Anomalous fetus
5. Other causes of increased pelvic blood flow like Pelvic inflammatory disease, ectopic pregnancy, non trophoblastic pelvic malignancy, uterine arteriovenous malformations.

METHODOLOGY:

The patients satisfying inclusion criteria were evaluated the day before evacuation of the uterus. This evaluation included:

1. Clinical assessment involving general, abdominal and bimanual pelvic examination.
2. Serum level of β-hCG.
3. Uterine artery Doppler velocimetry – uterine artery resistance index (UARI)

Then evacuation was done by the means of suction evacuation and specimens were sent for histopathology.

All the cases were given low dose combined oral contraceptive pills after evacuation of the molar pregnancy.

In the follow-up examination post evacuation Uterine artery resistance index was recorded 48 hours after evacuation of the uterus and post evacuation serial β-hCG levels monitored at 48 hours, 2^{nd},4^{th} and 8^{th} week respectively.

Uterine artery examination (both on the right and left sides) was done using Transabdomonal probe with pulsed and colour Doppler facilities by our institutional radiologist.

The β-hCG levels were correlated with uterine artery resistance index and statistical analysis was done using SPSS version 16 and Microsoft Excel 2007.

Groups

Groups	Definition	Number
MP Resolution	Without Invasive mole progression	36
MP Progression	With Invasive mole progression	4

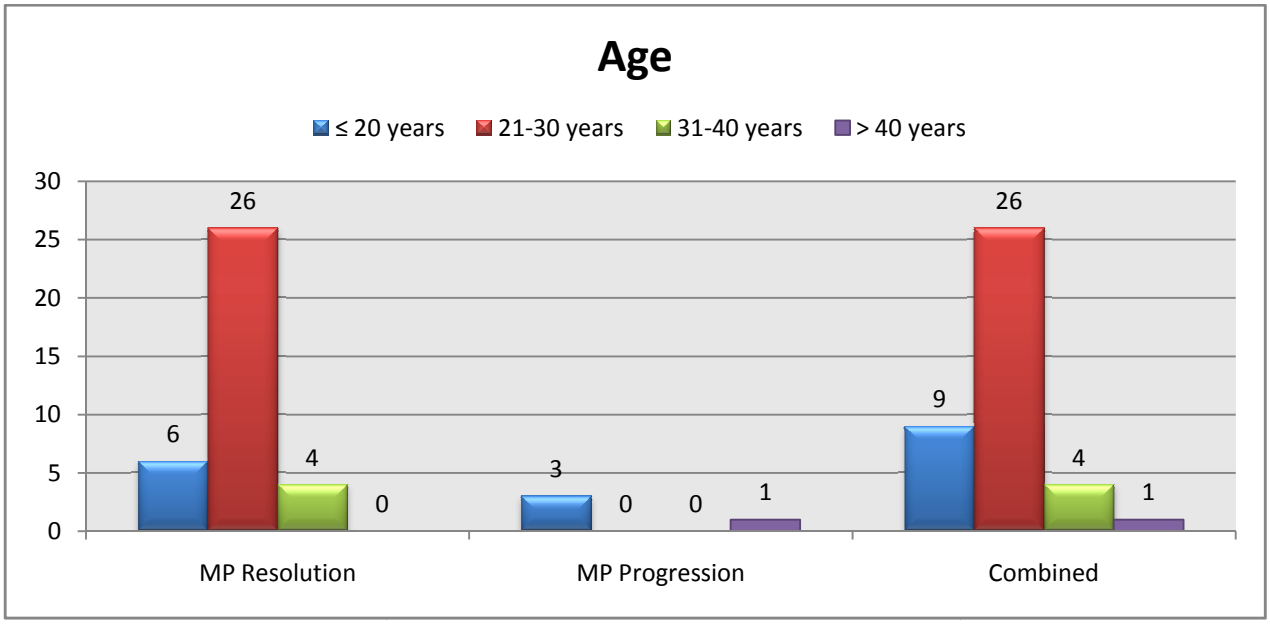
Null Hypothesis

Null Hypothesis : H0	UARI equal to ßHCG Doppler in predicting the resolution of molar pregnancy earlier
Alternate Hypothesis : H1	UARI better than ßHCG Doppler in predicting the resolution of molar pregnancy earlier

Data Analysis

Descriptive statistics was done for all data and were reported in terms of mean values and percentages. Suitable statistical tests of comparison were done. Continuous variables were analyzed with the unpaired t test. Categorical variables were analyzed with the Chi-Square Test and Fisher Exact Test. Statistical significance was taken as $P < 0.05$. The data was analyzed using SPSS version 16 and Microsoft Excel 2007.

Age

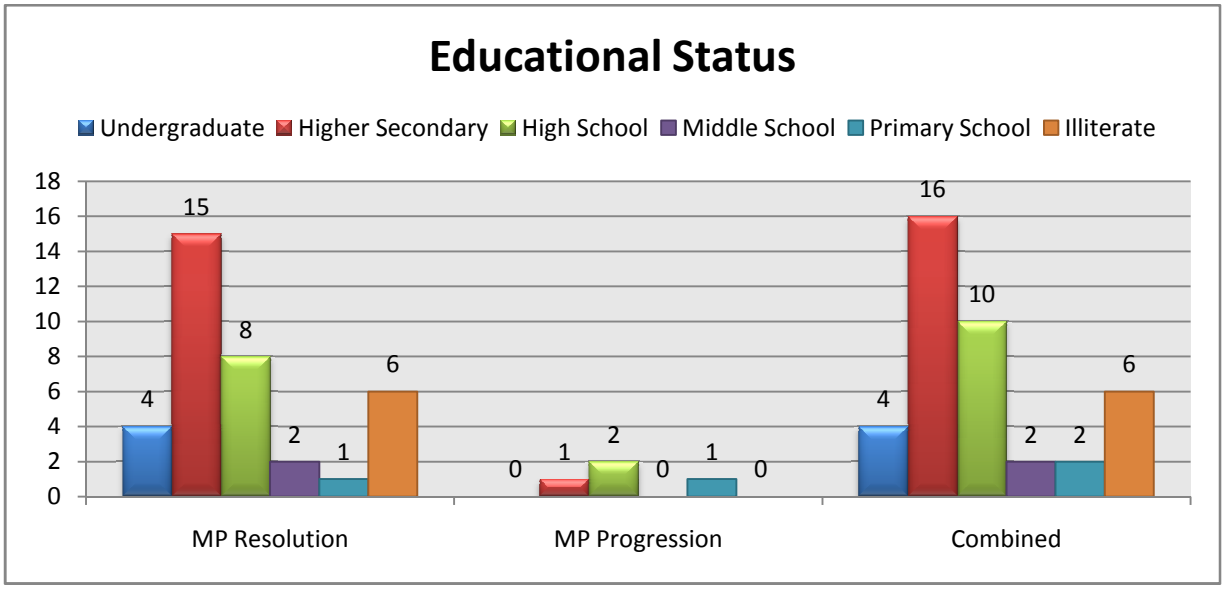


Age	MP Resolution	MP Progression	Combined	MP Resolution %	MP Progression %	Combined %
≤ 20 years	6	3	9	16.67	75.00	22.50
21-30 years	26	0	26	72.22	0.00	65.00
31-40 years	4	0	4	11.11	0.00	10.00
> 40 years	0	1	1	0.00	25.00	2.50
Total	36	4	40	100	100	100

Age Distribution	MP Resolution	MP Progression	Combined
Mean	24.69	26.50	24.875
SD	4.57	10.88	5.30
P value Unpaired t Test			0.5252

Among the study patients, there was no statistically significant difference in relation to age distribution between MP resolution group (mean=24.69, SD=4.57) and MP progression group (mean=26.50, SD=5.30) with a p value of >0.05 as per unpaired t test. Therefore we fail to reject the null hypothesis that there is no difference in age distribution between the study groups.

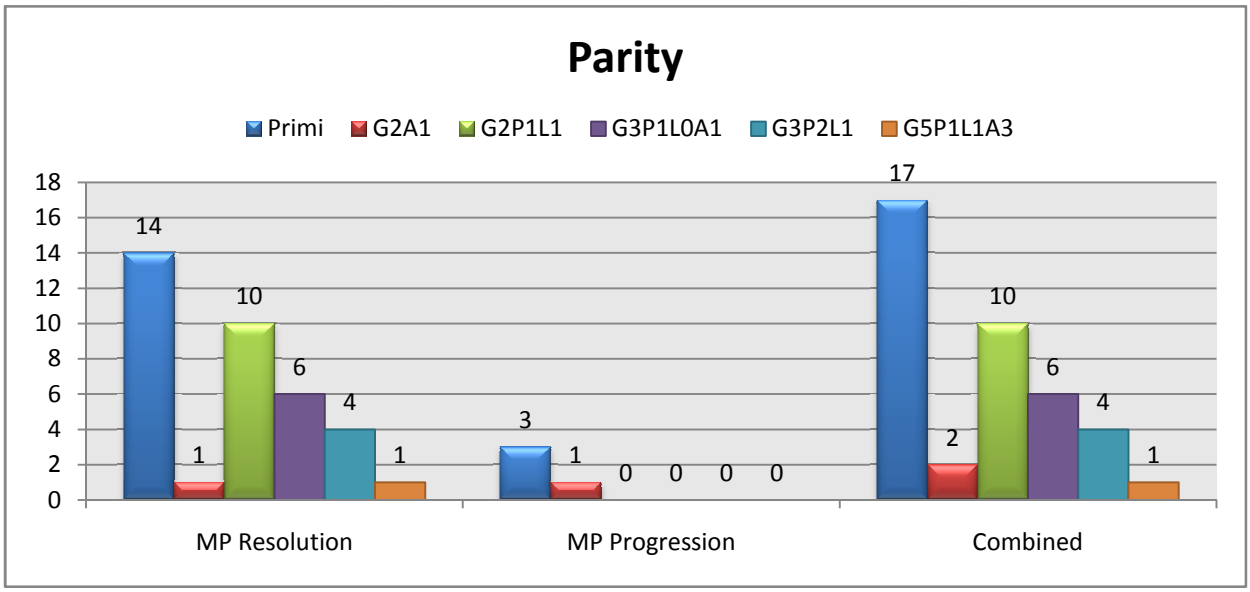
Educational Status



Educational Status	MP Resolution	MP Progression	Combined	MP Resolution %	MP Progression %	Combined %
Undergraduate	4	0	4	11.11	0.00	10.00
Higher Secondary	15	1	16	41.67	25.00	40.00
High School	8	2	10	22.22	50.00	25.00
Middle School	2	0	2	5.56	0.00	5.00
Primary School	1	1	2	2.78	25.00	5.00
Illiterate	6	0	6	16.67	0.00	15.00
Total	36	4	40	100	100	100
P value Chi Squared Test				0.2831		

Among the study patients, there was no statistically significant difference in relation to educational status between MP resolution group (mainly higher secondary- 41.67% followed by illiterate 16.67%) and MP progression group (mainly high school – 50.00% followed by higher secondary school – 25%) with a p value of >0.05 as per chi squared test. Therefore we fail to reject the null hypothesis that there is no difference in educational status between the study groups.

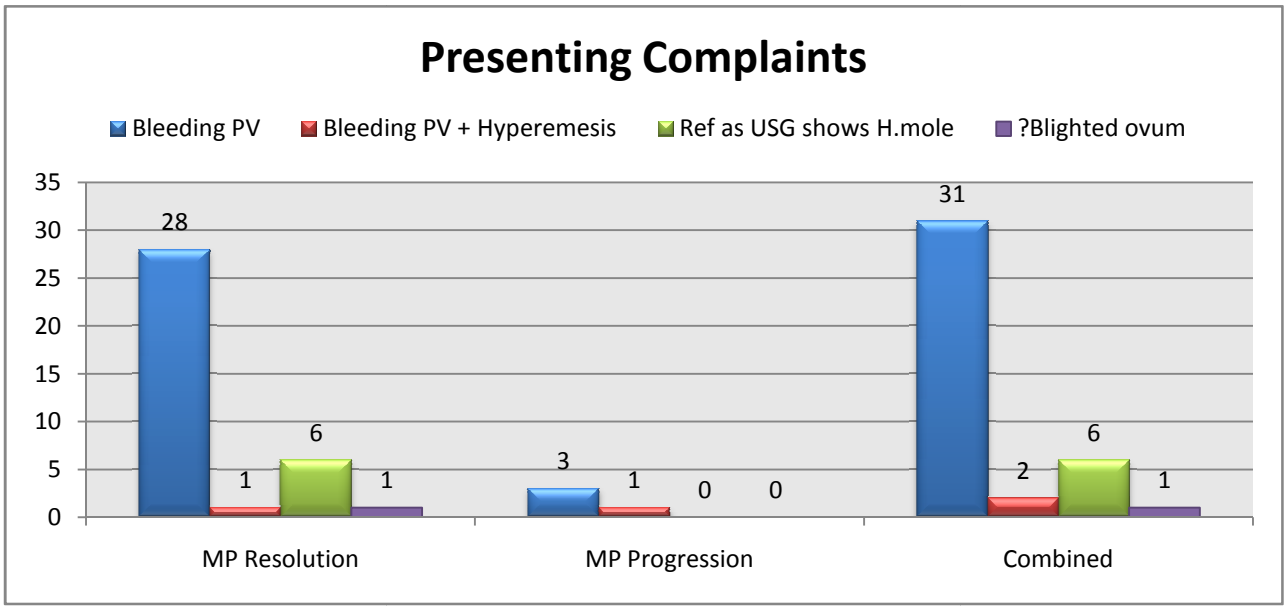
Parity



Parity	MP Resolution	MP Progression	Combined	MP Resolution %	MP Progression %	Combined %
Primi	14	3	17	38.89	75.00	42.50
G2A1	1	1	2	2.78	25.00	5.00
G2P1L1	10	0	10	27.78	0.00	25.00
G3P1L0A1	6	0	6	16.67	0.00	15.00
G3P2L1	4	0	4	11.11	0.00	10.00
G5P1L1A3	1	0	1	2.78	0.00	2.50
Total	36	4	40	100	100	100
P value Chi Squared Test				0.2211		

Among the study patients, there was no statistically significant difference in relation to parity status between MP resolution group (mainly primi-38.89% followed by G2P1L1 27.78%) and MP progression group (mainly primi – 75.00% followed by G2A1 – 25%) with a p value of >0.05 as per chi squared test. Therefore we fail to reject the null hypothesis that there is no difference in parity status between the study groups.

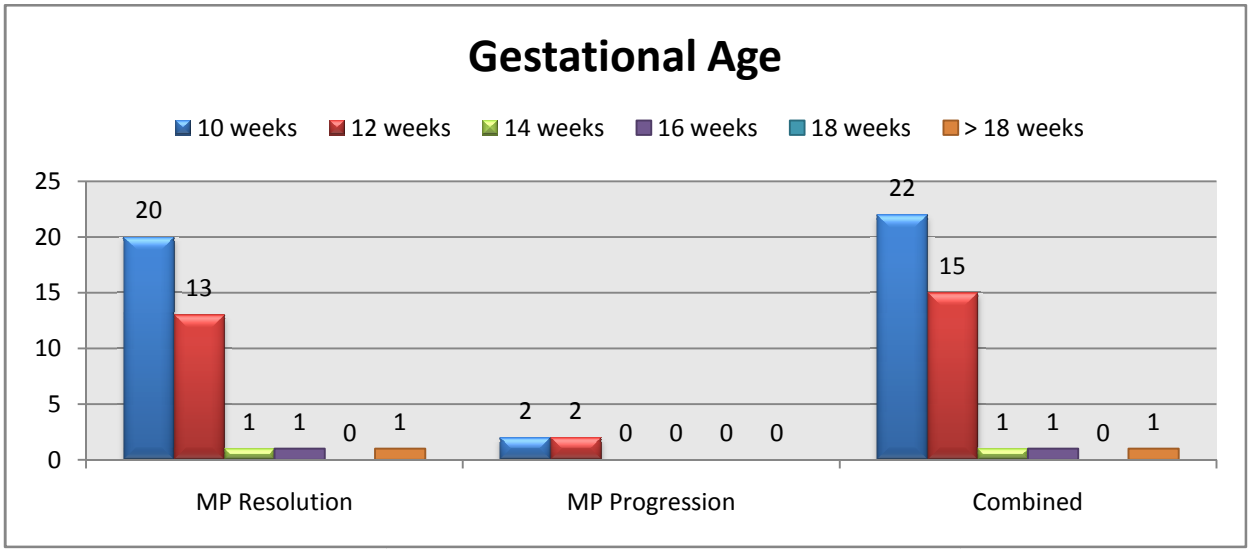
Presenting Complaints



Presenting Complaints	MP Resolution	MP Progression	Combined	MP Resolution %	MP Progression %	Combined %
Bleeding PV	28	3	31	77.78	75.00	77.50
Bleeding PV + Hyperemesis	1	1	2	2.78	25.00	5.00
Ref as USG shows H.mole	6	0	6	16.67	0.00	15.00
?Blighted ovum	1	0	1	2.78	0.00	2.50
Total	36	4	40	100	100	100
P value Chi Squared Test				0.2274		

Among the study patients, there was no statistically significant difference in relation to presenting complaints status between MP resolution group (mainly bleeding PV-77.78% followed by USG reference – 16.67%) and MP progression group (mainly bleeding PV – 75.00% followed by bleeding PV and hyperemesis – 25%) with a p value of >0.05 as per chi squared test. Therefore we fail to reject the null hypothesis that there is no difference in presenting complaints status between the study groups.

Gestational Age

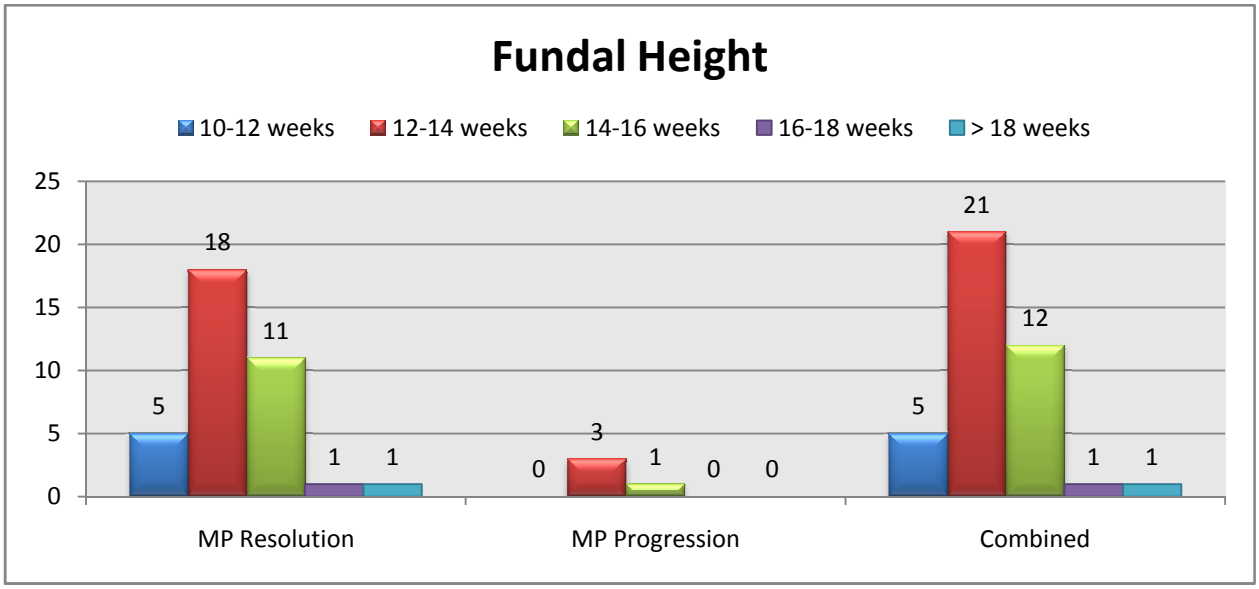


Gestational Age	MP Resolution	MP Progression	Combined	MP Resolution %	MP Progression %	Combined %
10 weeks	20	2	22	55.56	50.00	55.00
12 weeks	13	2	15	36.11	50.00	37.50
14 weeks	1	0	1	2.78	0.00	2.50
16 weeks	1	0	1	2.78	0.00	2.50
18 weeks	0	0	0	0.00	0.00	0.00
> 18 weeks	1	0	1	2.78	0.00	2.50
Total	36	4	40	100	100	100

Gestational Age Distribution	MP Resolution	MP Progression	Combined
Mean	11.19	11.00	11.175
SD	1.91	1.15	1.84
P value Unpaired t Test			0.8439

Among the study patients, there was no statistically significant difference in relation to gestational age distribution between MP resolution group (mean – 11.19, Sad – 1.91) and MP progression group (mean – 11.-00, SD – 1.15) with a p value of >0.05 as per chi squared test. Therefore we fail to reject the null hypothesis that there is no difference in gestational age distribution between the study groups.

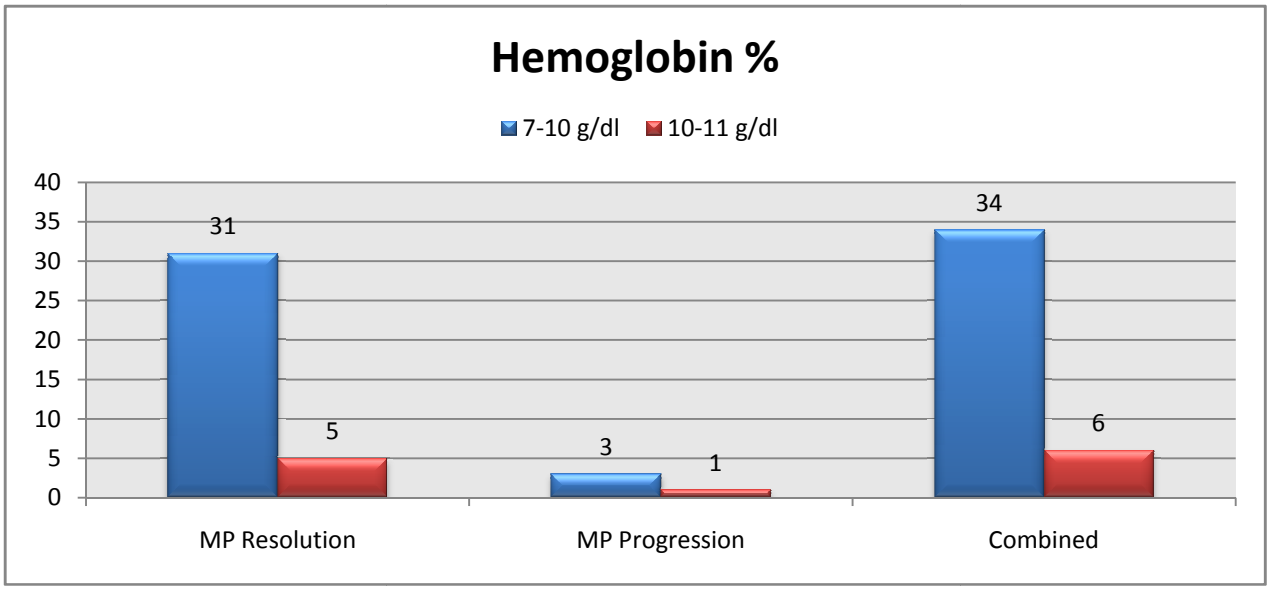
Fundal Height



Fundal Height	MP Resolution	MP Progression	Combined	MP Resolution %	MP Progression %	Combined %
10-12 weeks	5	0	5	13.89	0.00	12.50
12-14 weeks	18	3	21	50.00	75.00	52.50
14-16 weeks	11	1	12	30.56	25.00	30.00
16-18 weeks	1	0	1	2.78	0.00	2.50
> 18 weeks	1	0	1	2.78	0.00	2.50
Total	36	4	40	100	100	100
P value Chi Squared Test				0.8712		

Among the study patients, there was no statistically significant difference in relation to fundal height between MP resolution group (mainly 12-14 weeks – 50.00% followed by 14-16 weeks – 30.56%) and MP progression group (mainly 12-14 weeks – 75.00% followed by 14-16 weeks – 25.00%) with a p value of >0.05 as per chi squared test. Therefore we fail to reject the null hypothesis that there is no difference in fundal height status between the study groups.

Hemoglobin

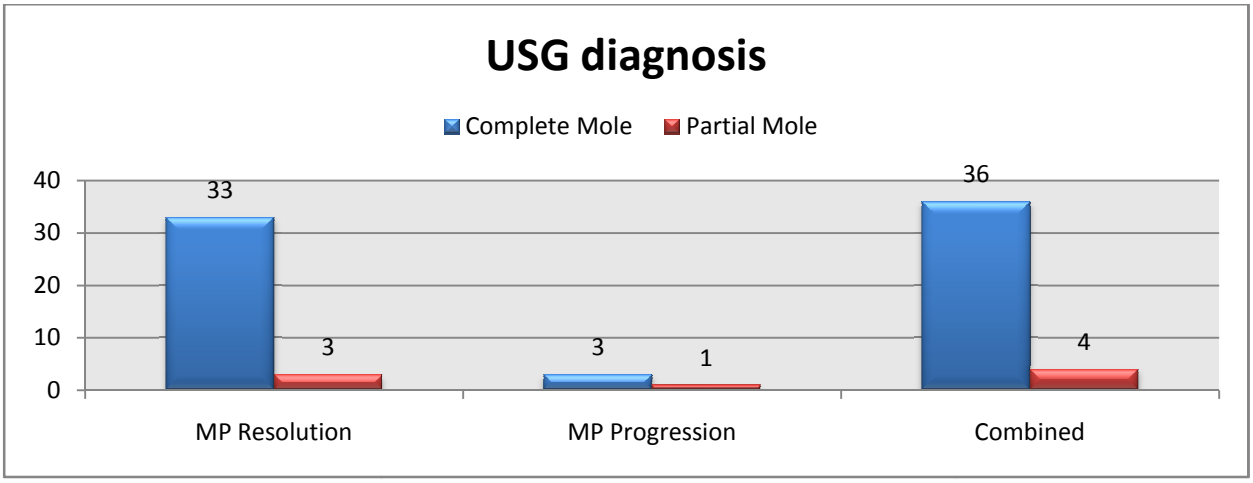


Haemoglobin %	MP Resolution	MP Progression	Combined	MP Resolution %	MP Progression %	Combined %
7-10 g/dl	31	3	34	86.11	75.00	85.00
10-11 g/dl	5	1	6	13.89	25.00	15.00
Total	36	4	40	100	100	100

Haemoglobin Distribution	MP Resolution	MP Progression	Combined
Mean	8.38	8.60	8.405
SD	1.01	1.24	1.02
P value Unpaired t Test			0.6922

Among the study patients, there was no statistically significant difference in relation to Hemoglobin distribution between MP resolution group (mean – 8.38, SD – 1.01) and MP progression group (mean – 8.60, SD – 1.24) with a p value of >0.05 as per chi squared test. Therefore we fail to reject the null hypothesis that there is no difference in Hemoglobin distribution between the study groups.

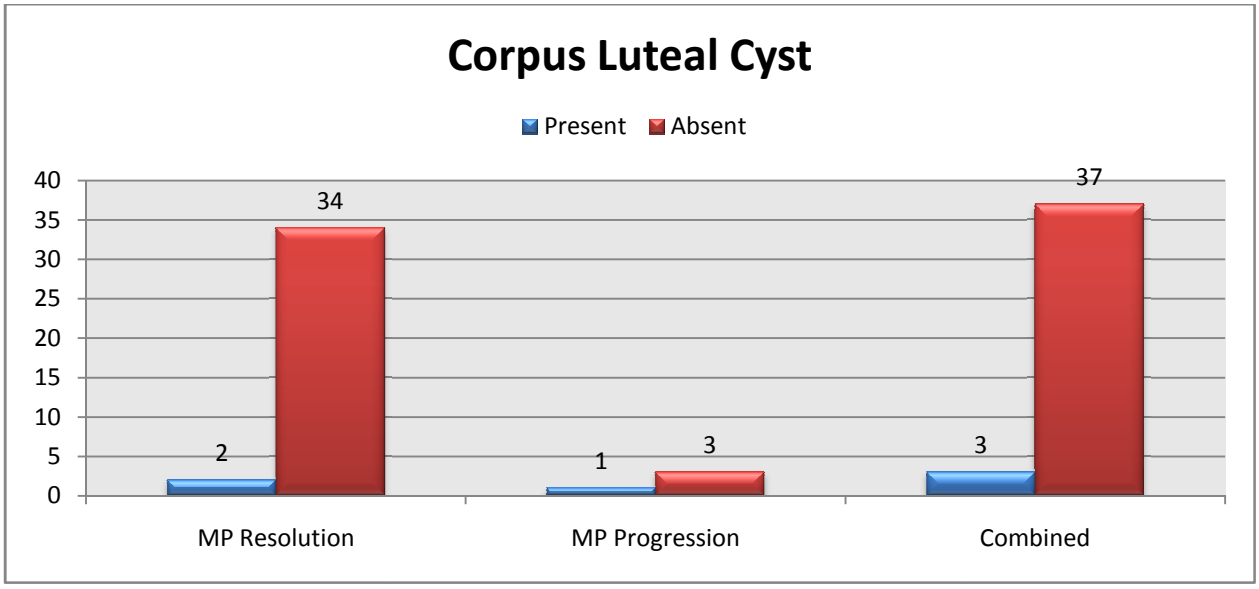
USG diagnosis



USG diagnosis	MP Resolution	MP Progression	Combined	MP Resolution %	MP Progression %	Combined %
Complete Mole	33	3	36	91.67	75.00	90.00
Partial Mole	3	1	4	8.33	25.00	10.00
Total	36	4	40	100	100	100
P value Chi Squared Test				0.2822		

Among the study patients, there was no statistically significant difference in relation to USG diagnosis status between MP resolution group (mainly complete mole – 91.47% followed by partial mole – 8.33%) and MP progression group (mainly complete mole – 75.00% followed by partial mole – 25.00%) with a p value of >0.05 as per chi squared test. Therefore we fail to reject the null hypothesis that there is no difference in USG diagnosis status between the study groups.

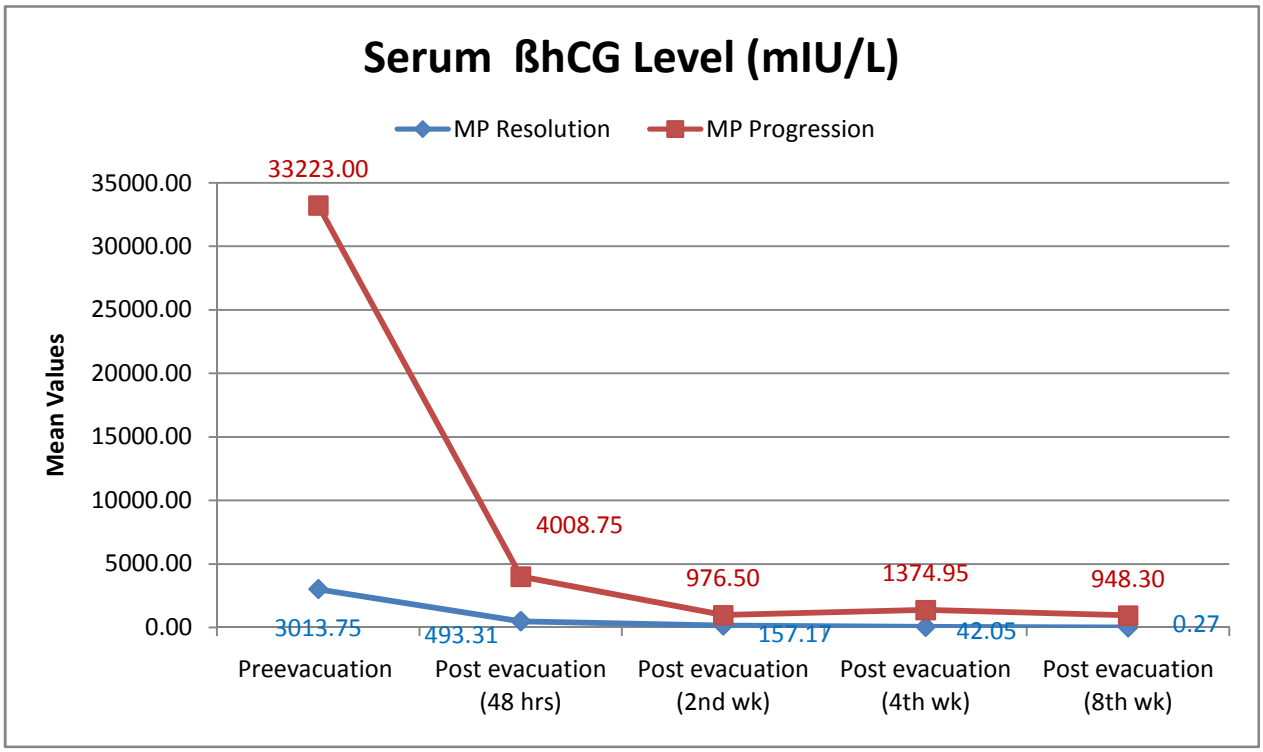
Corpus Luteal Cyst



Corpus Luteal Cyst	MP Resolution	MP Progression	Combined	MP Resolution %	MP Progression %	Combined %
Present	2	1	3	5.56	25.00	7.50
Absent	34	3	37	94.44	75.00	92.50
Total	36	4	40	100	100	100
P value Chi Squared Test				0.1618		

Among the study patients, there was no statistically significant difference in relation to corpus luteal cyst status between MP resolution group (mainly absent – 94.44% followed by present – 5.56%) and MP progression group (mainly absent – 75.00% followed by present – 25.00%) with a p value of >0.05 as per chi squared test. Therefore we fail to reject the null hypothesis that there is no difference in corpus luteal cyst status between the study groups.

Serum ßhCG Level



Serum ßhCG Level (mIU/L)		Preevacuation	Post evacuation (48 hrs)	Post evacuation (2nd wk)	Post evacuation (4th wk)	Post evacuation (8th wk)
MP Resolution	Mean	3013.75	493.31	157.17	42.05	0.27
	SD	5972.95	393.98	146.28	28.85	0.33
MP Progression	Mean	33223.00	4008.75	976.50	1374.95	948.30
	SD	54580.16	5871.20	105.12	1231.10	1366.00
P value Unpaired t Test		0.0012	0.0003	<0.0001	<0.0001	<0.0001

Among the study patients, there was a statistically significant difference in relation to serum ßhCG levels distribution between MP resolution group (mean – 741.31, SD 1272.17) and MP progression group (mean – 8106.30, SD – 11757.16) with a p value of <0.05 as per unpaired t test test. Therefore we reject the null hypothesis that there is no difference in serum ßhCG levels distribution between the study groups.

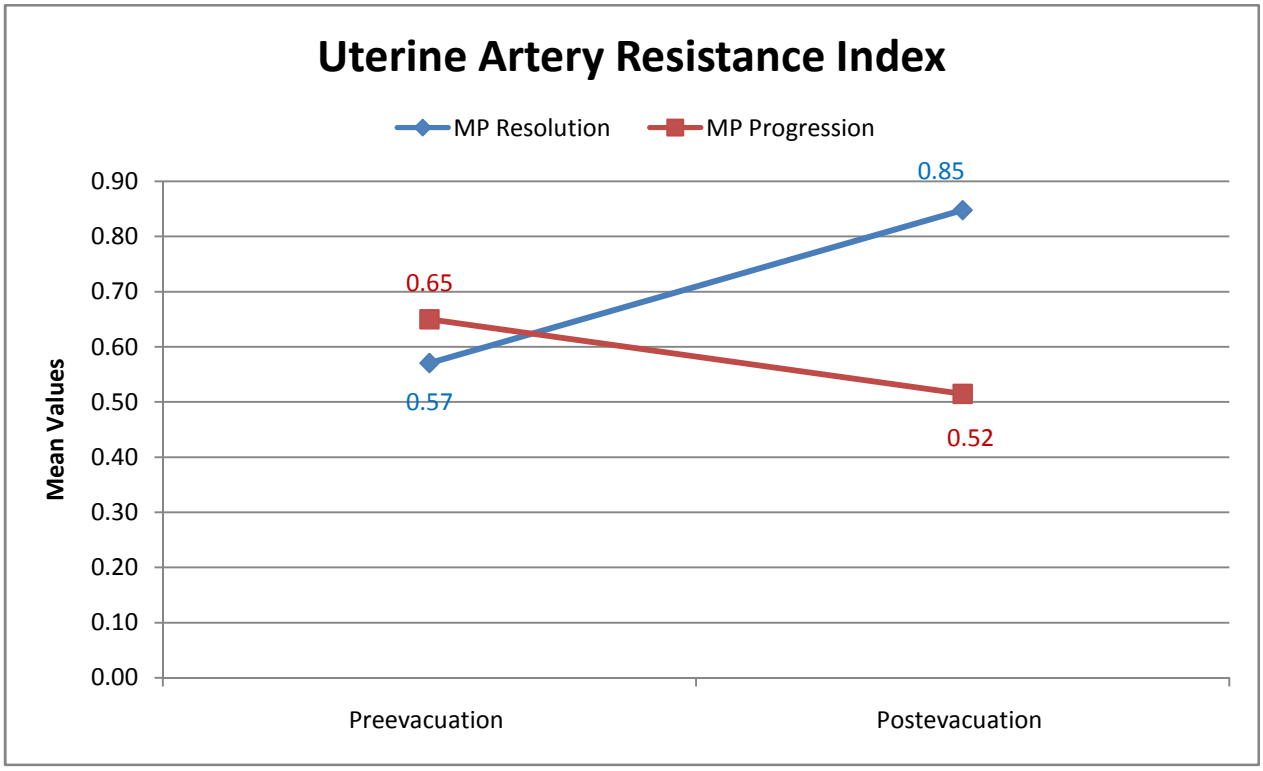
Discussion

The mean serum ßhCG levels were significantly lesser in MP resolution group compared to MP progression group by a mean difference of 7364.99 mIU/L (91% lesser). During the preevacuation period there was a 11 times increase in tire of mean serum ßhCG levels in MP progression group compared to MP resolution group which came down to 8 times increase in 48 hrs post evacuation period, 6 times increase in 2nd week post evacuation period and started to increase to 33 times more in 4^{th} week post evacuation period and finally it was 3838 times increased at 8^{th} week post evacuation period. This difference is significant with a p-value of 0.0003 as per unpaired t-test.

Conclusion

In this study we can safely conclude that in MP progression group there is sustained elevation of serum ßhCG levels compared to MP resolution group in patients with molar pregnancy

Uterine Artery Resistance Index



Uterine Artery Resistance Index		Preevacuation	Post evacuation	P value Paired t Test
MP Resolution	Mean	0.57	0.85	<0.0001
	SD	0.06	0.07	
MP Progression	Mean	0.65	0.52	0.0414
	SD	0.06	0.09	
P value Unpaired t Test		0.0182	<0.0001	

Among the study patients, there was a statistically significant difference in relation to uterine artery resistance index distribution between MP resolution group (mean – 0.71, SD 0.06) and MP progression group (mean – 0.58, SD – 0.07) with a p value of <0.05 as per unpaired t test . Therefore we reject the null hypothesis that there is no difference in uterine artery resistance index distribution between the study groups.

Discussion

The mean uterine artery resistance index was significantly higher in MP resolution group compared to MP progression group during postevcuation period by a mean difference of 0.33 (39% higher). This difference is significant with a p-value of <0.0001 as per unpaired t-test.

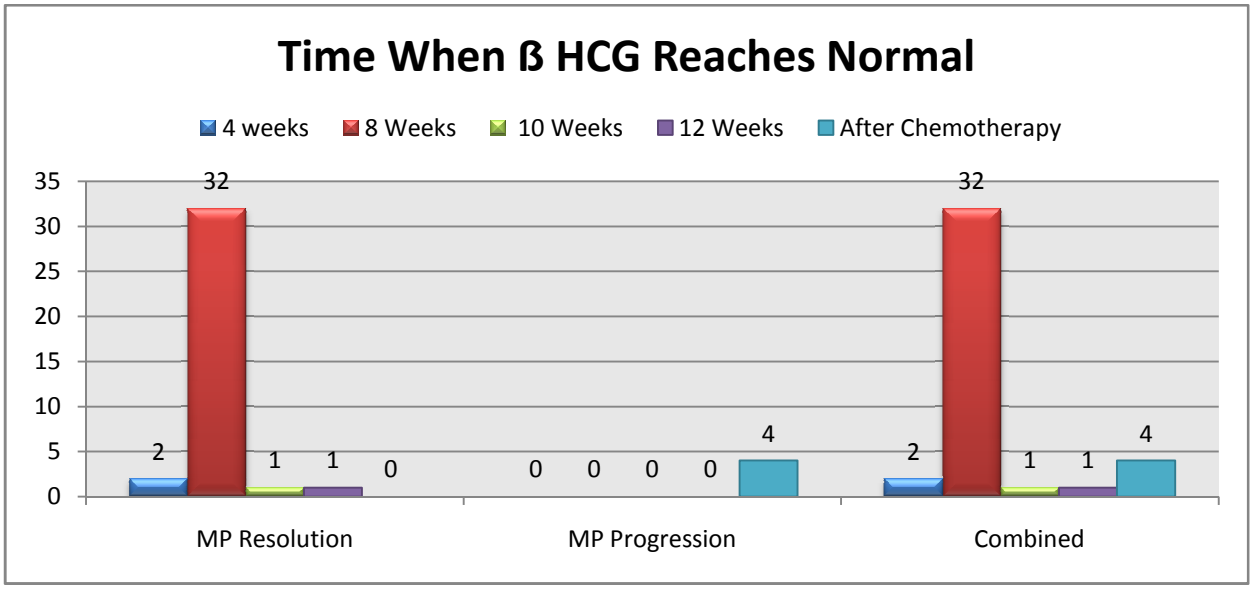
The mean uterine artery resistance index was significantly lower in MP resolution group during preevacuation compared to post evacuation period by a mean difference of 0.28 (33% higher). This difference is significant with a p-value of <0.0001 as per paired t-test.

The mean uterine artery resistance index was significantly higher in MP progression group during preevacuation compared to post evacuation period by a mean difference of 0.14 (21% higher). This difference is significant with a p-value of 0.0414 as per paired t-test.

Conclusion

In this study we can safely conclude that uterine artery resistance index has an inverse relationship in molar pregnancy pre and post evacuation. In MP progression group it significantly decreases in post evacuation period. But in MP resolution group it significantly increases in post evacuation period.

Time When ß HCG Reaches Normal



Time When ß HCG Reaches Normal	MP Resolution	MP Progression	Combined	MP Resolution %	MP Progression %	Combined %
4 weeks	2	0	2	5.56	0.00	5.00
8 Weeks	32	0	32	88.89	0.00	80.00
10 Weeks	1	0	1	2.78	0.00	2.50
12 Weeks	1	0	1	2.78	0.00	2.50
After Chemotherapy	0	4	4	0.00	100.00	10.00
Total	36	4	40	100	100	100
P value Chi Squared Test				<0.0001		

Among the study patients, there was a statistically significant difference in relation to time when ß HCG reaches normal between MP resolution group (mainly at 8 weeks – 88.89%) and MP progression group (mainly after chemotherapy – 100%) with a p value of <0.05 as per chi squared test. Therefore we reject the null hypothesis that there is no difference in time when ß HCG reaches normal status between the study groups.

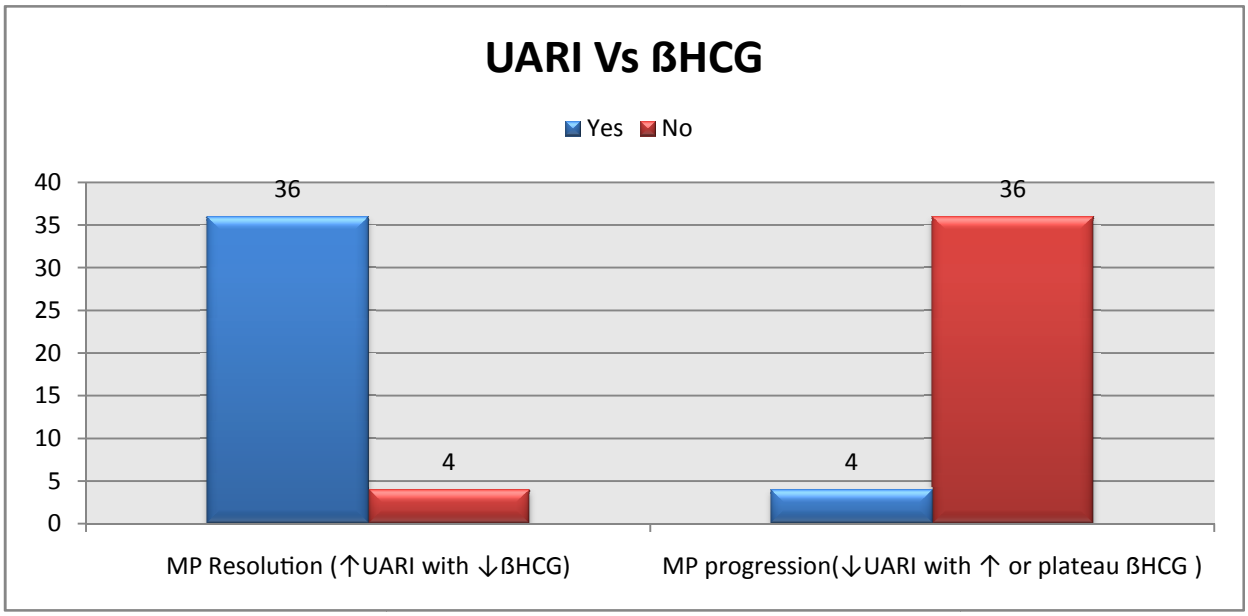
Discussion

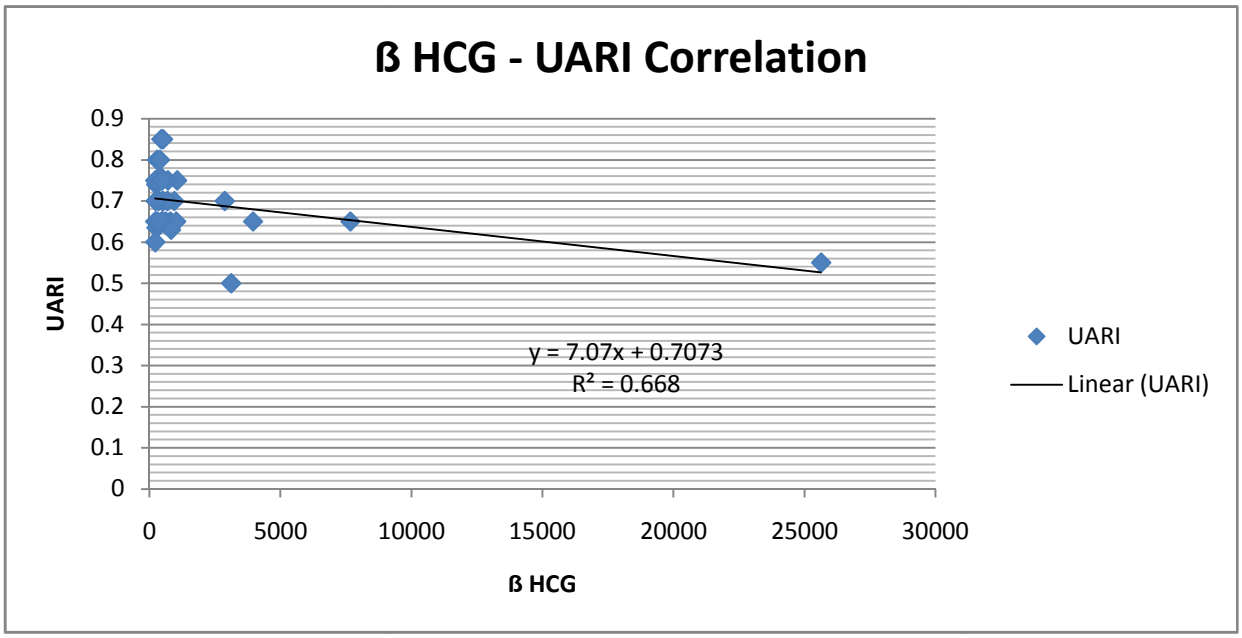
Majority of the patients in MP resolution group had time when ß HCG reaches normal between 4- 8 weeks (94.44%). Majority of the patients in MP progression group had time when ß HCG reaches normal only after chemotherapy (94.44%). The incidence of ß HCG reaching normal (within 8 weeks) was significantly higher in MP resolution group compared to MP progression group a percentage difference of 88.89% (94% higher). This difference is significant with a p-value of <0.0001 as per chi squared-test.

Conclusion

In this study we can safely conclude that ß HCG returns to normal quicker in MP resolution group compared to MP progression group among patients with molar pregnancy.

UARI Vs ßHCG


UARI Vs ßHCG
Yes
No
40
35
30
25
20
15
10
5
0
36
4
4
36
MP Resolution (↑UARI with ↓ßHCG)
MP progression(↓UARI with ↑ or plateau ßHCG)


ß HCG - UARI Correlation
UARI
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0
5000
10000
15000
20000
25000
30000
ß HCG
y = 7.07x + 0.7073
R² = 0.668
UARI
Linear (UARI)

UARI Vs ßHCG	MP Resolution (↑UARI with ↓ßHCG)	MP progression(↓UARI with ↑ or plateau ßHCG)	MP Resolution (↑UARI with ↓ßHCG) %	MP progression(↓UARI with ↑ or plateau ßHCG) %
Yes	36	4	90.00	10.00
No	4	36	10.00	90.00
Total	40	40	100	100
P value Chi Squared Test			<0.0001	

Pearson's "r" Correlation	-0.709896
P value One way ANOVA Test	**0.0086**

Among the study patients, there was a statistically significant difference between uterine artery resistance index and ß HCG levels in relation MP resolution group (↑UARI with ↓ßHCG – 90.00%) and MP progression group (↓UARI with ↑ or plateau ßHCG – 90.00%)with a p value of <0.05 as per chi squared test. Therefore we reject the null hypothesis that there is no difference in UARI Vs ßHCG status between the study groups.

Discussion

The incidence of ↑UARI with ↓ßHCG was significantly higher in MP resolution group compared to MP progression group by a percentage difference of 80.00% (89% higher). The incidence of (↓UARI with ↑ or plateau ßHCG was significantly higher in MP progression group compared to MP resolution group by a percentage difference of 80.00% (89% higher). This difference is significant with a p-value of <0.0001 as per chi squared-test.

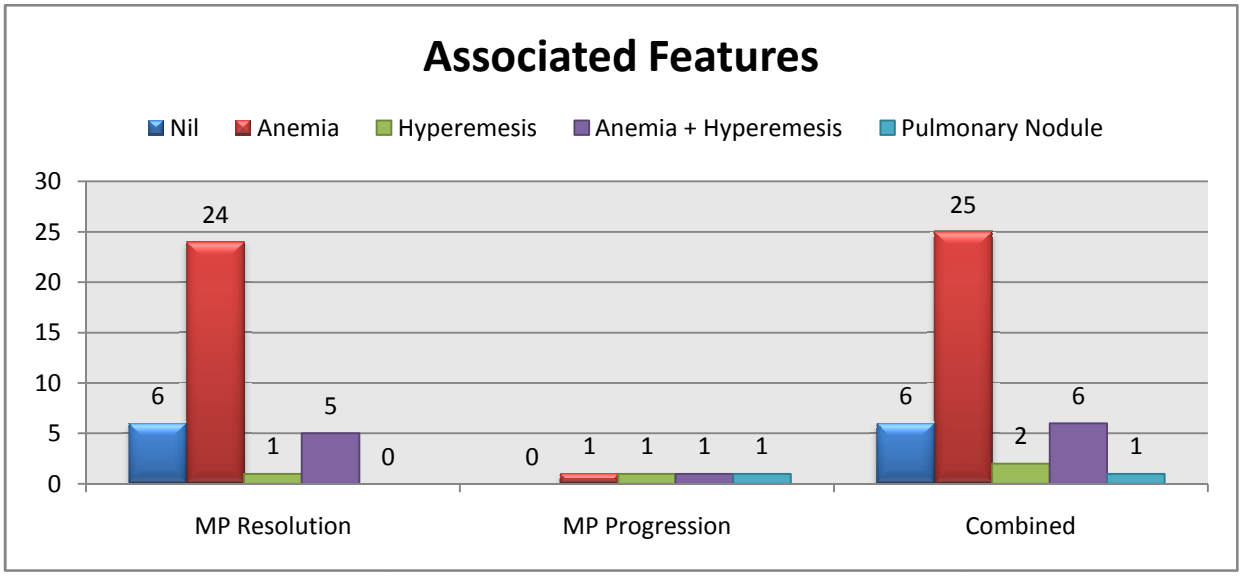
The increase in levels of UARI correlates negatively and strongly with the decrease in ßHCG levels. This is true 71% of times as per Pearson's "r" Correlation coefficient of -0.709896. For every 0.1 % increase in levels of UARI there is a corresponding 7.78 % decrease in ßHCG level. This is indicated by the linear correlation formula y = (7.07x) +0.7073. Since R2is 0.668, "the fitted regression equation explains 67% of the variation in Y"(Y= 7.07(ßHCG level) + 0.7073).

Thus 1 measurement increase in UARI causes 77.80 mIU/L decrease in ßHCG levels. This variation in UARI measurement in relation to ßHCG levels correlates 71% of times and this variation is truly accounted 67% of times.

Conclusion

In this study we can safely conclude that variation in UARI measurement in relation to ßHCG levels correlates strongly, inversely and negatively.

Associated Features



Associated Features	MP Resolution	MP Progression	Combined	MP Resolution %	MP Progression %	Combined %
Nil	6	0	6	16.67	0.00	15.00
Anaemia	24	1	25	66.67	25.00	62.50
Hyperemesis	1	1	2	2.78	25.00	5.00
Anaemia + Hyperemesis	5	1	6	13.89	25.00	15.00
Pulmonary Nodule	0	1	1	0.00	25.00	2.50
Total	36	4	40	100	100	100
P value Chi Squared Test				0.0062		

Among the study patients, there was a statistically significant difference in relation to occurrence of associated features between MP resolution group and MP progression group with a p value of <0.05 as per chi squared test. Therefore we reject the null hypothesis that there is no difference in occurrence of associated features status between the study groups.

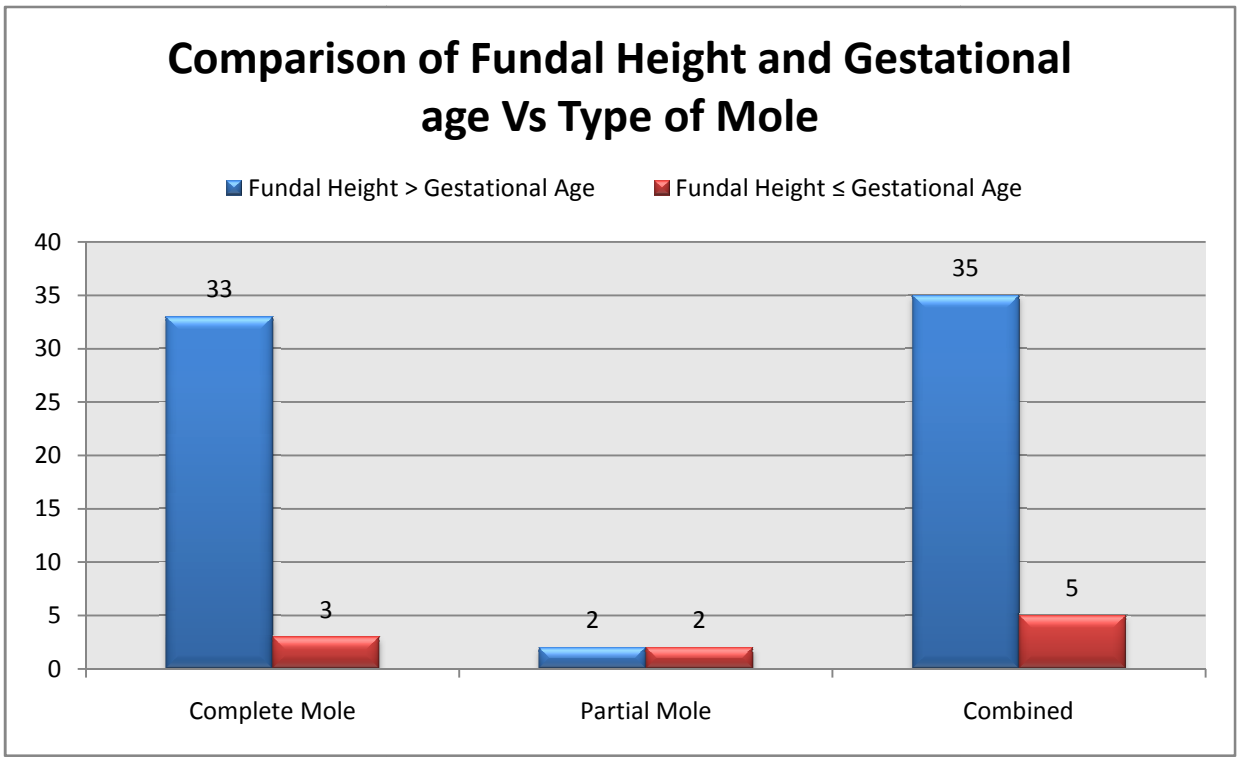
Discussion

Majority of the patients in MP resolution group had anemia as the main associated feature (66.67%). Majority of the patients in MP progression group had anemia, hyperemesis and pulmonary nodule as the main associated features (25.00%). The occurrence of associated features was significantly lower in MP resolution group compared to MP progression group a percentage difference of 83.33% (80% higher). This difference is significant with a p-value of 0.0062 as per chi squared-test.

Conclusion

In this study we can safely conclude that in MP progression group occurrence of associated features is more common compared to MP resolution group among patients with molar pregnancy.

Comparison of Fundal Height and Gestational age Vs Type of Mole



Comparison of Fundal Height and Gestational age Vs Type of Mole	Complete Mole	Partial Mole	Combined	MP Resolution %	MP Progression %	Combined %
Fundal Height > Gestational Age	33	2	35	91.67	50.00	87.50
Fundal Height ≤ Gestational Age	3	2	5	8.33	50.00	12.50
Total	36	4	40	100	100	100
P value Fishers Exact Test				0.0491		

Among the study patients, there was a statistically significant difference in comparison of fundal height and gestational age vs. type of mole with a p value of <0.05 as per chi squared test. Therefore we reject the null hypothesis that there is no difference in comparison of fundal height and gestational age vs. type of mole.

Discussion

Majority of the patients with complete mole had fundal height measurements greater than gestational age (91.67%). Majority of the patients with partial mole had fundal height measurements greater than gestational age (50.00%). The occurrence of fundal height measurements greater than gestational age status was significantly higher in complete mole group compared to partial mole group a percentage difference of 41.67% (45% higher). This difference is significant with a p-value of 0.0491 as per chi squared-test.

Conclusion

In this study we can safely conclude that complete mole presents significantly higher with fundal height measurements greater than gestational age compared to partial mole among patients with molar pregnancy.

DISCUSSION

ß hcg has been an excellent tool for diagnosing and monitoring therapeutic response in GTD, the average time around which β-hCG reverts back to normal is around 8-9 weeks in the post evacuation period. But routine follow up till this period may not be possible due to loss of compliance. In our study, patients with molar pregnancy were subjected to uterine artery Doppler study before and after evacuation and the efficacy of uterine artery resistance index in predicting resolution or persistence of disease earlier than β-hCG was observed.

1. Maternal Age:

In our study the age group of patients was between 18 to 42 years, with the mean age being 24 yrs.Persistence of molar pregnancy was observed in extremes of age group <20 & >40 yrs.

N.J.sebire et al in 2002 conducted an observational study of maternal age distribution from a large scale retrospective obstetric database over a 12 year period and he reported that extremes of maternal age had positive relationship for risk of molar pregnancy due to defective oocyte.

2. Educational Status:

In our study there was no significant difference in the educational status of people with either resolution or progression of molar pregnancy.

3. Parity:

In our study 17 patients were primi para, 10 were G2P1L1, 6 patients had history of 1 previous miscarriage and 1 patient had 3 previous miscarriages, there is no significant difference in the parity status of both groups.

4. Presenting Complaints:

In our study, 31 patients presented with bleeding per vaginum, one patient with hyperemesis, six patients were referred as sonographically detected molar pregnancy and one as blighted ovum. Bleeding per vaginum was the most common presenting symptom among both the groups.

5. Gestational Age:

The mean gestational age of presentation was 11 weeks in our study group, since prenatal care is sought much earlier nowadays.

6. Fundal Height Larger For Gestational Age:

In our study, the occurrence of fundal height greater than gestational age status was significantly higher in complete mole group compared to partial mole group. Larger uterine size for dates is seen due to trophoblastic hyperplasia and hemorrhage.

7. Hemoglobin:

The mean hemoglobin level in our study group was around 8.3%, vaginal bleeding was severe enough to cause symptomatic anemia and most of these patients were transfused in the pre evacuation period.

8. USG Diagnosis:

In our study sonographically diagnosed complete mole was seen in 36 patients and partial mole in 4 patients, which correlated with histopathological examination of products of conceptus.

9. Corpus Luteal Cyst:

In our study occurrence of corpus luteal cyst was observed in 3 patients due to elevated circulating ß hcg levels and the cyst resolved in the post evacuation period

10.ßhCG Levels:

In our study, The mean serum ßhCG levels was significantly lesser in MP resolution group compared to MP progression group by a mean difference of 7364.99 mIU/L (91% more lesser). During the preevacuation period there was a 11 times increase in tire of mean serum ßhCG levels in MP progression group compared to MP resolution group which came down to 8 times in 48 hrs post evacuation period, 6 times in 2nd week post evacuation period and started to increase to 33 times more in 4^{th} week post evacuation period and finally it was 3838 times increased at 8^{th} week post evacuation period.

11. Uterine Artery Resistance Index:

In our study, the mean uterine artery resistance index was significantly higher in MP resolution group compared to MP progression group during postevcuation period by a mean difference of 0.33 (39% higher).

The mean uterine artery resistance index was significantly higher in MP progression group during preevacuation compared to post evacuation period.

This fall in UARI in the MP progression group in the post evacuation period is due to the inherent character of trophoblast to invade and destroy uterine vasculature, forming low resistance lacunas .Similar observation was made by Maymon et al,that there was a fall in the UARI in the post evacuation visit of people with persistent molar pregnancy

12. Time When ßhcg Reaches Normal:

In our study, Majority of the patients in MP resolution group had time when ß HCG reaches normal between 4- 8 weeks. Majority of the patients in MP progression group had time when ß HCG reaches normal only after chemotherapy.

Cameron et al observed that it would take around 4-12 weeks for ßhcg to reach normal values in the post evacuation period.

13. UARI With ßhCG:

In our study, the incidence of ↑UARI with ↓ßHCG was significantly higher in MP resolution group compared to MP progression group by a percentage difference of 80.00% the incidence of ↓UARI with ↑ or plateau ßHCG was significantly higher in MP progression group compared to MP resolution group by a percentage difference of 80.00%. Thus 1 measurement increase in UARI causes 77.80 mIU/L decreases in ßHCG levels. The increase in levels of UARI correlates negatively and strongly with the decrease in ßHCG.

Similar observation were made by Kawano et al and Chan et al that ↑UARI was associated with ↓ßHCG in the post molar evacuation.

14. Associated Features:

Majority of the patients in MP resolution group had anemia as the main associated feature (66.67%). Majority of the patients in MP progression group had anemia, hyperemesis and pulmonary nodule as the main associated features (25.00%). The occurrence of associated features was significantly lower in MP resolution group compared to MP progression group a percentage difference of 83.33%.

SUMMARY

- This study was conducted in Department of obstetrics and gynecology, Government Rajaji Hospital, Madurai Medical College, Madurai. The study was conducted to observe the role of uterine artery Doppler in earlier prediction of resolution or persistence of molar pregnancy
- 40 patients of molar pregnancy were observed, resolution was seen in 36 patients, persistence of molar pregnancy was seen in 4 patients.
- There was a significant fall in post evacuation ß-hCG values in patients with resolution of molar pregnancy and rise in post evacuation ß-hCG values in patients with progression of molar pregnancy.
- The average time for the ß-hCG values to become normal was around 4-8 weeks in the molar pregnancy resolution group, while in patients with persistence ß-hCG values became normal only after chemotherapy.
- There was a significant fall in post evacuation UARI in patients with persistence of molar pregnancy, while there was a significant rise in the post evacuation UARI in patients with resolution of molar pregnancy.
- A strong correlation is observed with the post evacuation rise in UARI with fall in ß hcg and vice versa.

CONCLUSION

In our study we concluded that Uterine Artery Resistance Index (UARI) is a non invasive,reproducible and reliable diagnostic approach in earlier prediction of resolution or persistence of Gestational Trophoblastic Disease in conjunction with βhCG.

BIBLIOGRAPHY

1. Berek & Novak's Gynecology, 15th edition – Chapter 39, Gestational Trophoblastic Disease. 1458 – 1476.
2. Howkin's & Bourne, Shaw's text book of gynecology, 16th edition - Chapter 19, Gestational Trophoblastic Disease.311-320.
3. WHO classification of tumors of female reproductive organs ,4th edition-volume 6.
4. Neda Salih Amin, F.R.C.S. (Ed), Rasha Najah Yassen, F.I.C.M.S - Uterine Artery Doppler Blood flow in Cases of Hydatidiform Mole and its Correlation with β-hCG, Iraqi J. Comm. Med., Jan. 2014 (1).
5. Qi Zhou, MD, Xiao-Ying Lei, MD, Qing Xie, MD,Jim D. Cardoza, MD Sonographic and Doppler Imaging in the Diagnosis and Treatment of Gestational Trophoblastic Disease, J Ultrasound Med 2005; 24:15–24.
6. Lawrence H. Lin,* Lisandra S. Bernardes, Eliane A. Hase, Koji Fushida, Rossana P.V. Francisco - Is Doppler ultrasound useful for evaluating gestational trophoblastic disease - CLINICS 2015;70(12):810-815.
7. Mahrooz Malek et al, Complementary Role of Ultrasound in Management of Gestational Trophoblastic Disease - Iran J Radiol. 2015 April; 12(2): e13955.
8. Diaa Eldeen M Abd El Aal et al – Uterine artery Doppler flow in cases of hydatiform mole and its correlation with β hCG, dx.doi.org/10.1016/S0301-2115(03)00282-3.

9. R Agarwal et al, Uterine artery pulsatility index: a predictor of methotrexate resistance in gestational trophoblastic neoplasia British Journal of Cancer (2012) 106(6), 1089 – 1094.
10. The Ultrasound of life, Ultrasound of complete molar pregnancy http://www.fetalultrasound.com/online/text/12-019.HTM.
11. Lazarus E, Hulka C, Siewert B, Levine D. Sonographic appearance of early complete molar pregnancies. J Ultrasound Med 1999; 18: 589–94.
12. Use of uterine artery doppler flow velocimetry for the prediction of gestational trophoblastic neoplasia after complete hydatidiform mole *repositorio.unesp.br/bitstream/handle/11449/.../000866746.pdf?...1*
13. Amit kyal et al, Use of uterine artery doppler flow velocimetry for the Prediction of gestational trophoblastic neoplasia after Complete hydatidiform mole,10-5005/jp-journals-10006-1247.
14. Sunita Dhanda et al, Gestational Trophoblastic Disease: A Multimodality Imaging Approach with Impact on Diagnosis and Management Radiology Research and Practice, Volume 2014, Article ID 84275.
15. Barry W. Hancock. Gestational Trophoblastic Diseases. Obstetrics and Gynecology an evidence based text for MRCOG 2004: 756-761.
16. J.G. Grudzinskas. Miscarriage, ectopic pregnancy and trophoblastic disease. Dewhurst's Textbook of Obstetrics and Gynaecology for Postgraduate. Sixth edition 1999: 61-75.
17. F. Gary Cunningham, Paul C. MacDonald, Norman F. Gant et al. Placental Disorders. Williams Obstetrics 20th.Edition (1997):657-693.

18. Alan H. DeCherney, Lauren Nathan. Gestational Trophoblastic Diseases. Current Obstetrics and Gynecology. Ninth edition (2002):933-959.
19. William F. Ganong. Function of the Reproductive System. Review of Medical Physiology.18th Edition (2003):386-434.
20. Fox H. Female reproductive system. In: Anderson MC (ed). Systemic Pathology. Vol 6. 3rd ed. New York, NY: Churchill Livingstone; 1991:435–445.
21. Wolf NG, Lang JM. Genetic analysis of gestational trophoblastic disease: a review. Semin Oncol 1995; 22:130–141.
22. Szulman AE, Surti U. The syndromes of hydatidiform mole, II: morphologic evaluation of the complete and partial mole. Am J Obstet Gynecol 1978; 132:20?
23. Green CL, Angtuaco TL, Shah HR, Parmley TH. Gestational trophoblastic disease: a spectrum of radiologic diagnosis. Radiographics 1996; 16:1371–1384.
24. Osamor JO, Oluwasola AO, Adewole IF. A clinicopathological study of complete and partial hydatidiform moles in a Nigerian population. J Obstet Gynaecol 2002; 22:423–425.
25. Chan F, Chau M, Pun T, Lam C, Ngan H,Wong R. A comparison of colou Doppler sonography and the pelvic arteriogram in assessment of patients with gestational trophoblastic disease. Br J Obs Gynaecol. 1995;102(9): 720-5, http://dx.doi.org/10.1111/j.1471-0528.1995.tb11430.x.

26. Jauniaux E, Nicolaides KH. Early ultrasound diagnosis and follow-up of molar pregnancies. Ultrasound Obstet Gynecol. 1997;9(1):17-21, http://dx.doi.org/10.1046/j.1469-0705.1997.09010017.x.
27. Yalcin OT, Ozalp SS, Tanir HM. Assessment of gestational trophoblastic disease by Doppler ultrasonography. Eur J Obs Gynecol Reprod Biol. 2002;103(1):83-7, http://dx.doi.org/10.1016/S0301-2115(02)00026-X.
28. Emoto M, Sadamori R. Clinical usefulness of contrast-enhanced color Doppler ultrasonography in invasive and noninvasive gestational trophoblasticdiseases: a preliminary study. J Reprod Med. 2011;56(5-6):224-34.
29. Tepper R, Shulman A, Altaras M, Goldberger S, Maymon R, Holzinger M, et al. The role of color Doppler flow in the management of nonmetastatic gestational trophoblastic disease. Gynecol Obs Invest. 1994;38(1):14-7, http://dx.doi.org/10.1159/000292436.
30. Abd El Aal DE, El Senosy ED, Kamel MA, Atwa M. Uterine artery Doppler blood flow in cases of hydatidiform mole and its correlation with beta-hCG. Eur J Obstet Gynecol Reprod Biol. 2003;111(2):129–34.
31. Niemann I, Petersen LK, Hansen ES, Sunde L. Predictors of low risk of persistent trophoblastic disease in molar pregnancies. Obstet Gynecol. 2006;107(5):1006–11.
32. Callen PW. Ultrasonography in obstetrics and gynecology. 5th edPhiladelphia: Elsevier; 2007.

33. Carter J, Fowler J, Carlson J, Saltzman A, Byers L, Carson L, et al. Transvaginal color flow Doppler sonography in the assessment of gestational trophoblastic disease. J Ultrasound Med. 1993;12(10):595–9.
34. Ayhan A, Tuncer ZS, Halilzade H, Kucukali T. Predictors of persistent disease in women with complete hydatidiform mole. J Reprod Med. 1996;41(8):591–4.
35. Agarwal R, Strickland S, McNeish IA, Patel DC, Foskett M, Boultbee JE, Newlands ES, Seckl MJ (2002) Doppler ultrasonography of the uterine artery and the response to chemotherapy in patients with gestational trophoblastic tumors. Clin Cancer Res 8: 1142–1147.
36. Bower M, Newlands ES, Holden L, Short D, Brock C, Rustin GJ Begent RH, Bagshawe KD (1997) EMA/CO for high-risk gestational trophoblastic tumors: results from a cohort of 272 patients. J Clin Oncol 15: 2636–2643.
37. McGrath S, Short D, Harvey R, Schmid P, Savage PM, Seckl MJ (2010) The management and outcome of women with post-hydatidiform mole 'low-risk' gestational trophoblastic neoplasia, but hCG levels in excess of 100 000 IU l(-1). Br J Cancer 102: 810–814.
38. Shih Ie M (2007) Gestational trophoblastic neoplasia–pathogenesis and potential therapeutic targets. Lancet Oncol 8: 642–650.
39. Bagshawe KD (1976) Risk and prognostic factors in trophoblastic neoplasia. Cancer 38: 1373–1385.
40. B. J. Wagner, P. J. Woodward, and G. E. Dickey, "From the archives of the AFIP. Gestational trophoblastic disease: radiologic- pathologic correlation," Radiographics, vol. 16, no. 1, pp. 131–148, 1996.

41. S. D. Allen, A. K. Lim, M. J. Seckl, D. M. Blunt, and A. W. Mitchell, "Radiology of gestational trophoblastic neoplasia," Clinical Radiology, vol. 61, no. 4, pp. 301–313, 2006.
42. T. Y. Ng and L. C. Wong, "Diagnosis and management of gestational trophoblastic neoplasia," Bailliere's Best Practice and Research in Clinical Obstetrics and Gynaecology, vol. 17, no. 6, pp. 893–903, 2003.
43. M. Bower, E. S. Newlands, L. Holden et al., "EMA/CO for highrisk gestational trophoblastic tumors: results from a cohort of 272 patients," Journal of Clinical Oncology, vol. 15, no. 7, pp. 2636–2643, 1997.
44. J. T. Soper, "Gestational trophoblastic disease," Obstetrics & Gynecology, vol. 108, no. 1, pp. 176–187, 2006.
45. Akoi S, Hata H, Hata K, et al. Doppler color flow mapping on an invasive mole. Gynecologic Obstet Invest 1989;27(1):52-4.
46. Tepper R, Shulman A,et al. The role of color Doppler flow in the management of nonmetastatic gestational trophoblastic disease. Gynecologic Obstet Invest 1994;38(1):14-7.
47. Hsieh FJ, Wu CC, Lee CN, et al. Vascular patterns of gestational trophoblastic tumors by color Doppler ultrasound 1994. Cancer 4(8):2361-5.

QUESTIONNAIRE

NAME: UNIT:

AGE: IP.NO:

OBSTETRIC CODE:

H/O PRESENTING ILLNESS:

ASSO FEATURES OF HYPERTHYROIDISM/GHT:

PAST HISTORY: H/O DM,HT,HEART DISEASE,HYPOTHYROIDISM

CHRONIC DRUG INTAKE:

MENSTRUAL HISTORY:

DATE OF LMP:

FAMILY HISTORY:

H/O CARCINOMA:

GENERAL EXAMINATION

HEIGHT: PEDAL EDEMA:

WEIGHT: SPINE:

ANEMIA: BREAST:

THYROID: GAIT:

SYSTEMIC EXAMINATION

PULSE: CVS:

BLOOD PRESSURE: RS:

PER SPECULAM: CNS:

PER VAGINUM: PER ABDOMEN:

INVESTIGATIONS:

Hb%

BLOOD GROUPING & TYPING

RBS

BLOOD UREA

SERUM CREATININE

LFT

URINE SUGAR

URINE ALBUMIN

USG ABDOMEN & PELVIS

CONSENT PAPERS

NAME: UNIT:

AGE: IP NO:

PRESENT HISTORY: LMP:

PAST HISTORY:

OBSTETRIC HISTORY:

Consent for uterine artery Doppler study in the pre&post evacuation period

---

ABBREVIATIONS

β –hCG: - Beta human chorionic gonadotropin

UARI : - Uterine Artery Doppler Resistance Index

USG : - Ultra sonogram

HD : - Hydatidiform mole

MP : - Molar pregnancy

CM : - Complete mole

PM : - Partial mole

GTN : - Gestational Trophoblastic Neoplasia

GTD : - Gestational Trophoblastic Disease

PSTT : - Placental Site Trophoblastic Tumor

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O
1													Post evacuation ßHCG		
2	S.No	Name	Age	Educational status	Parity	Presenting c/o	Gestational age	Fundal height	Hb %	USG diagnosis	Corpus Luteal cyst	Preevacuation ßHCG	48 hrs	2nd wk	4th wk
3	1	Meena	21	Higher secondary	G2P1L1	Bleeding PV	10 weeks	12-14 weeks	7.8	CM		3943	1020	302	15.7
4	2	Latha	18	10th	Primi	Bleeding PV	12 weeks	14-16 weeks	8	CM		2150	1016	976	3000
5	3	Sivaranjani	18	10th	Primi	Bleeding PV	10 weeks	12-14 weeks	7.6	CM		2612	763	122	22
6	4	Ambikavathy	27	BA	G3P1L1A1	Bleeding PV	11 weeks	12-14 weeks	8	CM		1892	206	145	30
7	5	Periyatchi	28	Degree holder	G2P1L1	Ref as USG shows H.mole	10 weeks	12-14 weeks	8.4	CM		1723	212	98	10
8	6	Poonkothai	26	B.Tech	G5P1L1A3	Ref as USG shows H.mole	10 weeks	12-14 weeks	7.8	CM		2145	324	76	12
9	7	Seetha	26	Higher secondary	G3P1L1A1	Bleeding PV	10 weeks	12-14 weeks	8	CM		976	201	98	16
10	8	Viayalakshmi	19	Higher secondary	Primi	Bleeding PV,Hyperemesis	10 weeks	12-14 weeks	10.2	CM		1385	378	76	24
11	9	Ashmath agina	18	10th	G2A1	Bleeding PV	16 weeks	16-18 weeks	7.8	CM		2067	216	119	52
12	10	Divya	24	Bsc	Primi	Bleeding PV	12 weeks	14-16 weeks	8	CM		1078	221	96	48
13	11	Pandiselvi	32	Higher secondary	G2P1L1	Bleeding PV	19 weeks	22 weeks	7.6	CM		3167	673	118	29
14	12	Jothi	22	10th	G2P1L1	Bleeding PV	10 weeks	12 weeks	10.6	Partial Mole		1343	503	76	4
15	13	Annakili	29	Higher secondary	G3P1L1A1	Bleeding PV	11 weeks	14-16 weeks	9.8	CM		1876	532	182	36
16	14	Pavithra	22	10th	G3P1L1A1	Bleeding PV	12 weeks	14-16 weeks	7.8	CM		1179	625	134	20
17	15	Mohanapriya	20	10th	Primi	Bleeding PV,Hyperemesis	10 weeks	12-14 weeks	10.4	CM		1290	382	1029	1360
18	16	Malar	26	8th	Primi	Bleeding PV	10 weeks	10-12 weeks	8.2	CM		986	276	86	18
19	17	Suganya	20	Higher secondary	Primi	Bleeding PV	14 weeks	12-14 weeks	10.4	Partial Mole		2006	876	114	68
20	18	Tamilselvi	22	Polytechnic	G3P1L1A1	Ref as USG shows H.mole	10 weeks	12-14 weeks	8.4	CM		1891	439	153	92
21	19	Nambuselvi	42	2nd	Primi	Bleeding PV	12 weeks	14 weeks	7.6	Partial Mole		114560	12768	830	17.8
22	20	Vijaya	35	Nil	G2P1L1	Bleeding PV	12 weeks	12-14 weeks	10	CM		1298	312	101	43
23	21	Muthupandi	29	Higher secondary	G2P1L1	Bleeding PV	12 weeks	14-16 weeks	8.2	CM		1786	301	165	89
24	22	Maharani	28	10th	G3P2L2	Bleeding PV	10 weeks	12-14 weeks	9.2	CM		2651	512	134	98
25	23	Mareeshwari	26	Higher secondary	G2P1L1	Bleeding PV	10 weeks	12 weeks	10.6	CM		889	219	97	29
26	24	Sundaravalli	33	Higher secondary	Primi	?Blighted ovum	10 weeks	12 weeks	10.2	CM	Yes	3012	1521	131	65
27	25	Suganya	22	Higher secondary	Primi	Ref as USG shows H.mole	10 weeks	16 weeks	7.6	CM		3298	1213	482	101
28	26	Panjavarnam	35	Higher secondary	G2P1L1	Bleeding PV	12 weeks	14-16 weeks	7.4	CM		2550	621	231	82
29	27	Nandhini	19	Polytechnic	G2A1	Bleeding PV	10 weeks	12-14 weeks	8.4	CM	Yes	14892	1869	1071	1122
30	28	Manonmani	19	10th	Primi	Bleeding PV	10 weeks	12-14 weeks	7.6	CM		912	201	82	21
31	29	Kaleeswari	22	10th	G2P1L1	Ref as USG shows H.mole	10 weeks	12-14 weeks	8	CM	Yes	12420	1275	610	60
32	30	Sundarammal	25	Nil	G3P2L1	Bleeding PV	12 weeks	14-16 weeks	7.6	CM		35980	1600	712	53
33	31	Selvi	27	10th	G3P2L1	Ref as USG shows H.mole	12 weeks	14-16 weeks	7.2	CM		1287	331	102	76
34	32	Bhavani	24	Higher secondary	Primi	Bleeding PV	10 weeks	12-14 weeks	8	CM		912	112	76	21
35	33	Bhagavathi	18	8th	Primi	Bleeding PV	12 weeks	14-16 weeks	8.2	CM		865	124	85	15
36	34	Meena	22	Higher secondary	G2P1L1	Bleeding PV	10 weeks	12-14 weeks	7.8	CM		1943	389	120	56
37	35	Malliga	21	Nil	G3P1L0A1	Bleeding PV	12 weeks	12 weeks	7.2	Partial Mole		954	110	43	2
38	36	Sudha	25	Nil	Primi	Bleeding PV	10 weeks	12-14 weeks	8.2	CM		1814	412	92	21
39	37	Eshwari	25	Higher secondary	Primi	Bleeding PV	12 weeks	14-16 weeks	7.8	CM		1487	412	121	76
40	38	Kavitha	28	Nil	G3P2L2	Bleeding PV	10 weeks	12-14 weeks	8	CM		1272	159	91	28
41	39	Priya	24	3rd	Primi	Bleeding PV	12 weeks	14-16 weeks	8.2	CM		1934	316	104	63
42	40	Sivarani	21	Nil	Primi	Bleeding PV	10 weeks	12-14 weeks	8.4	CM		962	154	84	18

	P	Q	R	S	T	U	V
1		**Uterine artery RI**					
2	**8th wk**	**Preevacuation**	**Postevacuation**	**ß HCG reaches normal at**	**MP Resolution (↑UARI with ↓ßHCG)**	**MP progression(↓UARI with ↑ or plateau ßHCG**	**Asso features**
3	0.1	0.6	0.9	8 Weeks	Yes	No	Anemia
4	2921	0.6	0.4	after chemotherapy	**NO**	**YES**	Anemia
5	0.1	0.6	0.9	8 Weeks	Yes	No	Anemia
6	<0.5	0.7	1	8 Weeks	Yes	No	Anemia
7	<0.2	0.6	0.92	8 Weeks	Yes	No	Anemia
8	<0.2	0.6	0.8	8 Weeks	Yes	No	Anemia
9	<0.1	0.58	0.9	8 Weeks	Yes	No	Anemia
10	<0.4	0.6	0.9	8 Weeks	Yes	No	Hyperemesis
11	<0.2	0.5	0.9	8 Weeks	Yes	No	Anemia
12	<0.5	0.6	1	8 Weeks	Yes	No	Anemia
13	0.4	0.5	0.8	12 Weeks	Yes	No	Anemia
14	<0.1	0.6	0.9	4 weeks	Yes	No	Nil
15	<0.4	0.5	0.9	8 Weeks	Yes	No	Nil
16	<0.1	0.7	0.9	8 Weeks	Yes	No	Anemia
17	58	0.7	0.56	after chemotherapy	**NO**	**YES**	Hyperemesis
18	<0.1	0.57	0.7	8 Weeks	Yes	No	Anemia
19	2	0.5	0.8	8 weeks	Yes	No	Nil
20	<0.1	0.7	1	10 Weeks	Yes	No	Anemia
21	2.2	0.6	0.5	after chemotherapy	**NO**	**YES**	pulmonary nodule
22	<0.4	0.6	0.8	8 Weeks	Yes	No	Nil
23	<0.1	0.5	0.8	8 weeks	Yes	No	Anemia
24	<0.4	0.6	0.8	8 Weeks	Yes	No	Nil
25	<0.4	0.5	0.8	8 Weeks	Yes	No	Nil
26	<0.1	0.6	0.8	8 Weeks	Yes	No	Hyperemesis
27	<0.4	0.5	0.8	8 weeks	Yes	No	Hyperemesis
28	<0.4	0.6	0.8	8 Weeks	Yes	No	Anemia
29	812	0.7	0.6	after chemotherapy	**NO**	**YES**	Anemia,hyperemesis
30	<0.1	0.6	0.8	8 Weeks	Yes	No	Anemia
31	0.2	0.6	0.8	8 Weeks	Yes	No	Anemia,Hyperemesis
32	0.4	0.5	0.8	8 Weeks	Yes	No	Hyperemesis
33	0.1	0.6	0.9	8 Weeks	Yes	no	Anemia
34	<0.2	0.6	0.9	8 Weeks	Yes	No	Anemia
35	<0.4	0.5	0.8	8 Weeks	Yes	No	Hyperemesis
36	0.1	0.5	0.8	8 Weeks	Yes	No	Anemia
37	<0.1	0.5	0.7	4 weeks	Yes	No	Anemia
38	<0.1	0.5	0.8	8 Weeks	Yes	No	Anemia
39	<0.1	0.6	0.9	8 Weeks	Yes	No	Anemia
40	<0.1	0.5	0.8	8 Weeks	Yes	no	Anemia
41	<0.1	0.6	0.9	8 Weeks	Yes	No	Anemia
42	<0.1	0.6	0.8	8 Weeks	Yes	No	Anemia